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TREATMENT OF RESPIRATORY FAILURE IN THE NEWBORN

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ALTHOUGH the infant and neonatal mortality rates have fallen considerably over the past thirty years, many infants are still dying in the newborn period because of respiratory failure. Clifford (2) states that asphyxia causes 58% of deaths in the newborn. Treatment is still unsatisfactory, and this paper will discuss the methods in use today, with a consideration of some of the facts upon which therapy is based.

A second reason for the importance of this subject is that there is a high incidence of behaviour and emotional problems and of mental retardation in those infants who survive an initial period of anoxia. Preston (3) followed up 132 patients with a birth history of anoxia, and found they all showed some behaviour difficulties in their early years, and in addition 35 had subnormal intelligence and 37 had epilepsy.

Cases of respiratory failure in the newborn may be grouped into

A. IMMEDIATE

(1) Mild—good muscle tone, resist movement of head and limbs, conjunctival reflex present.

(2) Moderate—muscle tone and reflexes poor or absent, heart sounds strong.

(3) Severe—completely flaccid, no response to any stimuli, heart sounds weak, slow and irregular.

B. DELAYED—breathe well at birth either spontaneously or after resuscitation, but after a period of some hours of good breathing the respirations became gradually more difficult and ultimately fail. These are probably chiefly cases of "hyaline membrane disease".

Hyaline membrane disease occurs most commonly in prematures, infants born of diabetic mothers, and infants born by Caesarian section. On microscopic section eosinophilic membranes are found lining the alveoli and alveolar ducts, and the latter are often filled with squamous epithelial cells and other debris. It is thought to result from aspiration of amniotic sac contents, with precipitation of the protein material as it dries during subsequent respiration. It is never found unless an infant has breathed for at least one hour.

The causes predisposing to failure of respiration include

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A. *Causes in the mother*: age over 35, primipara, profound anemia, toxemia or other severe illness, diabetes.
B. *Causes associated with delivery*: prolonged labor, excessive analgesia (especially nembutal) and anaesthesia, traumatic delivery, Caesarian section, placenta previa, abruptio placentae, umbilical cord short or knotted.
C. *Causes in the Fetus*: prematurity, congenital malformations, intracranial hemorrhage, erythroblastosis fetalis.

Some Facts Important to an Understanding of Therapy

(1) length of time the newborn can withstand hypoxia

It is generally agreed that the newborn can withstand hypoxia without permanent damage for a longer time than can the adult. The cerebral cortex may survive eight minutes hypoxia, whereas the medullary centres may survive twenty to thirty minutes. Between these times, hypoxia may result in a living baby but one with a permanently damaged cerebrum.

(2) occurrence of respiratory movements before birth

Many workers have observed fetal respiratory movements in animals and in the human. Davis and Potter (4) injected thorotrast into the amniotic sacs of women some hours before therapeutic abortion, and found even in the smallest (a 39 gm. fetus) that the dye was concentrated in the respiratory passages, often to such an extent that it outlined the pulmonary tree on X-Ray. They concluded that the fetus must make respiratory movements, and that amniotic fluid must be absorbed through the respiratory epithelium. Bonar and others (5) observed these movements directly in rabbits, dogs and rats, and found they were depressed by anesthetics given to the mother. Some authors have laid so much importance on these prenatal respiratory movements as to claim that postnatal difficulties can be attributed to defective respiratory movements in utero. However, the fetal movements are quite irregular, and may normally be absent for long periods of time, so it seems that such a claim is unjustified.

(3) appearance of lungs at birth

Farber and Wilson (6) have given a very clear description of the normal appearance of the lungs of newborns and the differences between the lungs of full-term and premature infants. In the lungs of stillborns at term, the alveoli are lined by high cuboidal epithelium, and the alveolar spaces are small. If much intrauterine respiratory effort has occurred more than the usual amount of amniotic fluid may be aspirated, and the alveoli may be somewhat distended, but the walls still have a wavy outline, and the epithelium is still high cuboidal. Once an alveolus expands, the lining cells become flattened, and do not subsequently become cuboidal even if the alveolus later collapses. They found, by examining the lungs of infants who survived varying lengths of time, and died of some cause other than pulmonary, that it takes from two to four days to open all the alveoli. This type of physiological atelectasis they call "initial atelectasis". In contrast to this is what they term "resorption atelectasis", which occurs when alveoli, which have once been fully expanded, collapse, usually as a result of obstruction in the proximal air passages. The alveoli then show slit-

like cavities, but the lining cells, as mentioned above, remain flat.

According to the newer concept (22), during the last 3 months of intrauterine life, the cells lining the alveolar wall became separated, and marked capillaries come in contact with the lumen. In this view, alveoli found to be lined by cuboidal epithelium at birth are quite immature.

In prematures, in addition to normal and unexpanded alveoli, there are found areas of epithelial cells which have not yet become organized into alveoli and so have no lumen. This represents a truly immature condition of the lung, and the extent of it varies directly with the prematurity of the infant. This is, of course, unexpandable tissue, and it may take two to six weeks for it to mature into alveoli and become capable of function.

(4) STIMULUS FOR THE FIRST BREATH

Cole (7) measured the time between the birth of the head and the initial respiratory gasp, and found that it usually occurred within 2 seconds, a cry within 5 seconds and regular respirations within 10 seconds. A delay of 30 seconds was definitely abnormal. The fact that it occurs so rapidly makes it reasonable to assume that cutaneous stimuli may be important, as there would not be much change in the O_2 or CO_2 tension of the blood reaching the respiratory centre in such a short time. Barcroft (8) showed in sheep fetuses that respiration thus readily initiated tends to be fairly regular and rhythmic. However, if the newborn is depressed by sedative or anesthetic, the first gasp may be delayed for some time after the cord is clamped, until either the O_2 tension falls or the CO_2 rises to such a degree that the respiratory centre is stimulated. This results in an irregular gasping type of respiration, quite different from that following simple cutaneous stimulation.

For decades there was much argument about whether the respiratory centre was stimulated by O_2 lack or CO_2 excess. Yandell Henderson (9) led the CO_2 school. He thought that if the respiratory center did not respond to the high CO_2 tension in the blood, the CO_2 should be raised even further by adding it in high concentration to the air being forced into the lungs. Eastman (10) has argued against this, and recent experience seems to support his contention that hypoxia is the underlying defect, that there is already too much CO_2 present, and that the initial treatment should consist of giving 100% O_2. He could find no relation between the onset of respiration and the CO_2 content of cord blood. He found the chief biochemical disturbances in asphyxia of the newborn to be: O_2 deficiency, CO_2 excess, excess of organic acids such as lactic, and severe acidosis, with a pH as low as 7.0. Others too have observed that respirations commence or improve when O_2 is given, whereas giving more CO_2 is without benefit and will increase the acidosis. Even if we do not know which is the important stimulus for the initiation of respiration, the important practical point is that the anoxic respiratory centre will not respond to any stimulus, and the urgent need is for O_2.

(5) DIFFICULTIES OF THE FIRST BREATH

At the moment of birth, there is obviously no air in the respiratory passages, but the bronchi and alveoli may contain more or less amniotic fluid. At one time it was thought that at the first breath all the alveoli opened completely and became filled with air. It was mentioned

above that this is not so, and it may take days, or even weeks in a premature infant, before they are all open.

With the first breath, the muscles of respiration must work not only against the elasticity of the lung tissue, but must overcome a very considerable surface tension effect due to the adhesion of the moist surfaces of the bronchioles and alveoli. This has been demonstrated in various ways.

Hermann (11), in 1879, showed that to expand the collapsed lungs of adult rabbits took an initial pressure of 12-20 cm. water, but subsequently 3-9 cm. pressure was sufficient.

Wilson and Farber (12) found much the same effect on lungs removed from rabbits and from stillborn infants. They applied a negative pressure outside the lungs and measured the air flow through the trachea by means of a spirometer. They found 15-25 cm. of water or more of negative pressure was required for the initial expansion, subsequently 12-15 cm. being sufficient.

This surface tension effect was demonstrated in a different way by Gruenwald (13). He cannulated the bronchus of a collapsed lung, and found that a pressure of 10-21 cm. water was required to force air into the lung, but saline solution expanded the lung at a pressure of only 5-10 cm. water. He then used a surface tension reducing agent (Amyl acetate), introduced and then removed, and after this he found the collapsed lung could be expanded with air at a lower pressure (7-16 cm. water).

These pressures may be compared with the pressure that a newborn is capable of achieving to expand his lungs. By placing a tight mask over the mouth and nose of newborn infants and connecting it to a manometer, Smith (14) has shown that full term infants and even some prematures can exert a negative pressure of 40-50 cm. water. The average negative pressure exerted by an adult on inspiration is about 95 cm. water.

So it is seen that the first breath requires a much greater pressure to expand the alveoli than do subsequent breaths, but that the healthy newborn is capable of achieving such pressures, with a considerable reserve of strength.

Another important factor which might be mentioned here is the power of the muscles of respiration and the rigidity of the chest wall. Breathing in young infants is chiefly diaphragmatic. If it is to be successful the bone and muscle framework of the chest must hold the chest rigid, otherwise when the diaphragm contracts the chest wall will simply cave in, and little negative pressure will be achieved. This difficulty arises chiefly in premature infants, and may be an important cause of their inability to achieve initial expansion, and later to provide sufficient tidal air for adequate oxygenation.

Treatment

When faced with an infant who fails to breathe at birth, we may be able from the obstetric history and from the progress of the delivery to guess at the cause, but often the respiratory failure is quite unexpected. The cause may be of such a serious nature that resuscitation will be impossible—e.g. severe intracranial hemorrhage, or complete immaturity of lungs or vital centers, but since we cannot tell the cause, we must proceed as though it were a remediable one, and give the infant the benefit of the doubt.

We might first mention methods which were once popular, but are now thought to be generally contraindicated.

(1) *Severe Cutaneous Stimuli.* Vigorous slapping, whirling the infant around, alternating hot and cold baths, have all been used, but may do real harm, and if breathing commences, it is more likely in spite of such manipulations than because of them. Gentle stimulation of the skin and movement of the joints may be of value in the milder cases.

(2) *Manual Artificial Respiration* is useless if no air has entered the lungs. It may force out a little fluid but there is nothing to produce the high negative pressure necessary to open the alveoli for the first time. It may help later on if respirations fail after the lungs have filled with air, and if the cause is not obstruction in the air passages.

(3) *Mouth to mouth insufflation.* The chief dangers are that too great a pressure will be produced, resulting in rupture of alveoli with possible production of pneumothorax, and infection. Also, the O_2 concentration is not very great. There is probably still a place for this method when other methods have failed or when no resuscitation equipment is at hand.

(4) *Use of Drugs.* This is another very controversial subject (15, 18). Drugs have been used either to initiate respirations, or to attempt to strengthen them when they have begun to weaken.

The three which have received the most favourable mention are as follows:

(*a*) Alpha-lobeline. This is best given I.V. into the umbilical vein, in dosage of 1/40 to 1/20 grain. It apparently acts through the chemoreceptors in the carotid body, and produces a deep gasping type of respiration. It acts within about 15 seconds of injection, and its action lasts for only a few minutes.

(*b*) Coramine (Nikethamide) is given I.M. in dosage of 2-4 minims. It acts through the same mechanism as lobeline, but for a longer time, and is probably better given after respirations have commenced.

The disadvantage of these drugs is that severely depressed chemo-receptors will not respond, and they may instead produce convulsions. Against this is the experience of Wilson *et al.* (15) who saw no undesirable effects from the use of lobeline in 340 newborns.

(*c*) Epinephrine has been injected into the heart when the heart sounds were absent or becoming faint and irregular, with occasionally good results.

Some writers feel that if the respiratory centre has been so damaged by hypoxia that it will not respond to the usual cutaneous or biochemical stimuli it is unlikely to respond to drugs. Certainly, if they are given in large doses they may do more harm than good, but Smith (14) feels that "they offer some possibility of turning the tide by producing a few gasps or increasing those already produced by the infant".

Having dispensed with methods which are either inadvisable or controversial, let us now turn to the methods which are in widespread use today.

(1) If there is any suspicion of the presence of asphyxia, one can *delay clamping the umbilical cord* till its pulsation has stopped. This will provide 100 cc. or more of blood for the infant, which will give it that much greater O_2-carrying capacity (19).

(2) *Warmth* must not be forgotten, as the newborn in respiratory failure may

also be in a shock-like condition and likely unable to maintain a normal temperature. The infant should be wrapped in warm blankets or kept in a heated environment like an incubator until regular respirators have been established.

(3) *Gentle handling* should be observed, as rough handling may contribute to shock or increase intracranial hemorrhage. Gentle cutaneous stimulation is not contra-indicated if the asphyxia is not severe.

(4) *Provision of a clear airway* is one of the most important procedures in every case. With a normal infant it is sufficient to clear out the mouth and pharynx by gentle suction with a mucus tube as soon as the baby is born, and preferably before the cord is clamped, as this is likely to provide an added stimulus for the first breath.

If no respiratory effort has been made after 1-2 minutes, or if the infant is obviously suffering severe asphyxia at the moment of birth, it has likely suffered a serious degree either of hypoxia or of narcosis, and may have aspirated large amounts of amniotic fluid or other material from the birth canal. It is therefore wise to apply suction to the larynx and trachea, and probably also the stomach. This is best done by visualizing the larynx directly with an infant laryngoscope, and passing a catheter through it.

A very useful apparatus for doing this has been developed by Dr. John Fletcher. It operates on the principle of an oxygen-powered atomizer, which provides at the same time oxygen and controlled suction, and is both light, compact and inexpensive. An endotracheal catheter is passed, and suction carried out by passing a plastic catheter through it. Oxygen can be supplied via a side-arm in the endotracheal catheter. Attached to the oxygen tube is a safety release valve which opens whenever the pressure exceeds 2½ cm. water, thus avoiding the danger of a high pressure rupturing alveoli of the lung.

If this or similar apparatus is not available one can pass any semi-flexible rubber or plastic catheter through the larynx, either with the aid of a laryngoscope or by guiding it with the finger, and clear the trachea by mouth suction.

(5) *Artificial Respiration.* If there has been no sign of spontaneous respiration, even after the stimulus of clearing the airway, then some method of artificial respiration must be used to get oxygen into the blood stream. It has been shown that some O_2 is absorbed through the skin, mucous membranes of the respiratory passages, and even through the stomach when oxygen has reached it, but none of these sources will provide sufficient to maintain life for more than a couple of hours. Two general methods are in use: (*a*) Positive pressure by face mask or endotracheal tube; (*b*) Negative pressure by Drinker respirator.

(*a*) Positive Pressure Methods. Using an endotracheal tube with side arm as described above, one can expand the lungs by intermittently pressing the thumb over the open end of the tube. The positive pressure in that apparatus does not exceed 2½ cm. water, though that could be raised by adjusting the pressure release valve. This would not be sufficient to overcome the surface tension effect if the lungs had not expanded, but sufficient O_2 might be absorbed from the trachea and bronchi to revive the chemo-receptors or respiratory centre and initi-

ate spontaneous respiration. When this has commenced, one can stop the intermittent pressure, and the O_2 concentration is then almost 72%. There is some advantage in having less than 100% O_2 at this stage, as the inert gases help to keep the open alveoli from collapsing.

There is considerable danger in using higher positive pressures. The effect of this is to open up a few alveoli, then over-expand them till they rupture, rather than opening up more and more unexpanded alveoli. Wilson (15) has stated that 16 cm. of water is the maximum safe pressure, and at 24.4 cm. pressure they found the lung tissue generally unexpanded with areas of over-expanded and ruptured alveoli.

Several mechanical positive-pressure machines have been widely used, some provide both positive and negative pressure. Their main disadvantage is their size and expense, and the difficulty of applying suction when needed. Martinez (16) used the Ericson and Johnson machine in 500 cases, and saw no harmful effects in the lungs of the nine autopsied babies (a total of 31 had died).

(*b*) Negative Pressure Methods. There are reports both in favor and against the use of an infant Drinker Respirator. Murphy (17) used a negative pressure of 8-10 cm. water, and found no evidence of injury to the respiratory tract in those who died, though more amniotic debris seemed to have accumulated in the alveoli than in a control group. With high negative pressures, the same danger holds as for positive pressures: overexpansion and rupture of some alveoli with failure to open up the others.

(6) *Aspiration of Stomach.* This procedure may help in preventing the delayed type of respiratory failure. The rationale is that amniotic fluid was swallowed in utero, and is vomited and aspirated after birth. On aspiration of the stomach, 5-20 cc. of amniotic fluid, often with thick mucus, may be obtained. The two groups in which this has been found of real benefit are infants born by Caesarian section and infants of diabetic mothers. Gellis said a year ago that they had had no cases of death due to delayed respiratory failure in the past 50 babies born to diabetic mothers. These babies had all had gastric suction performed at birth. Delayed respiratory failure used to be one of the commonest causes of death in these infants. They are also placed in incubators with O_2 and high water vapor concentration.

(7) *After-Care.* Following establishment of respirations, the infant should be kept in a warm environment with high O_2 and water vapor concentrations. This can be accomplished in an incubator, with the addition of a Nebulator or some other method of increasing the moisture content of the air. Pure O_2 is likely to have a very drying effect, and if nothing is done to combat this, hyaline membranes are more likely to form. The mouth and pharynx should be gently suctioned and the infant turned to the opposite side hourly, and nothing should be given by mouth for 12 to 24 hours.

The methods described will probably revive most asphyxiated newborns who are capable of being revived. None of

them, however, provides a substitute for the all-important initial inspiratory gasp. This problem is being attacked by a group in New York, their method consisting of a high positive pressure via the trachea for a fraction of a second, in an attempt to open up the alveoli in much the same manner as occurs with the normal first breath. Their work is still in the experimental stage, but some such approach may solve the present dilemma in which some infants get over-expansion and rupture of small portions of the lung, with no expansion of the rest.

Summary

In summary, the procedure which is most likely to revive a newborn infant suffering from respiratory failure consists of: mouth suction as soon as the head is born; delay clamping the umbilical cord until its pulsation stops; warmth and gentle handling at all times; gentle cutaneous stimulation; provision of a clear airway, including suction of any material in the trachea; insufflation of pure O_2 into the trachea; artificial respiration by either positive or negative pressure. Drugs such as lobeline and coramine may be used as a last resort. After breathing has commenced, the stomach should be aspirated. After-care consists of warmth, O_2 moisture, and giving nothing by mouth for 12 to 24 hours.

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A HAPPY AND PROSPEROUS NEW YEAR

AN AIR FORCE SUMMER INTERNESHIP*

By P/O M. BOCKNEK, 5T4, RCAF (Primary Reserve)

"Goose Bay, Labrador? No, No, there must be some mistake—please check the list again." Emphatically the voice came back over the phone—"130617, Pilot Officer M. Bocknek—Med/MO——— Goose Bay, Labrador!" And so with 2 fellow-Medics, Pilot Officers John Youngs 5T3 and Ian Kerr 5T5, I left for Montreal, Sunday midnight July 1/52, where we were to board the aircraft for Goose Bay. There exists at all RCAF Air Traffic Terminals the regulation that passengers must verify reservations at least 24 hours before takeoff time. Since the next scheduled flight for Goose was Mon. at 11:30 A.M., we were quite happy with the thought of not being able to comply with this regulation and so enjoy a few days in Montreal. But all we saw of Montreal was the phone book, for everything was ready and waiting for us; and we were booked on that morning's aircraft for Goose Bay.

When we took off, there was a persistent drizzle and it continued as far north as Mont Joli where we landed to refuel. From here to Goose was a flight over the most barren and mountainous country imaginable; and 6 hours and 20 minutes out of Dorval we landed at Goose Airport, the sun shining brightly for the first time that day. I recall alighting from the aircraft and stopping dead for before me stretched sand, scrubby pines, sand, buildings, and more sand. But this was to be home for 3½ months, so I closed my eyes and allowed myself to be transported to my quarters. Then the situation began to look brighter. I was assigned to a private room with running water, a spring mattress on the bed, a nice rug on the floor, and 2 draped windows overlooking the Nurses Quarters—so I decided to stay.

Goose Bay, Labrador, 813 air miles N.E. of Montreal is an all-year-round military Air Base which is home for R.C.A.F. (Royal Canadian Air Force) U.S.A.F. (United States Air Force) and D.O.T. (Department of Transport) personnel. Theoretically the station has two sides, Canadian and American, however no International Boundary exists and the only requisite for going from one side to the other is a mode of transport. The complement of Goose is quite large and growing more every day. Most of the married personnel have their wives and families with them, and the picturesque RCAF residential district of "Spruce Park" is composed of a new and ultra-modern concrete school (which handles all Canadian and American children in Grades I to XII) and the homes of the dependants. These homes are detached, oil-heated, electrically supplied, completely furnished (even to automatic clothes washers), and rent for a ridiculously low $40.00 per month.

Mail usually comes in 3 times weekly, fresh vegetables every Wednesday; and the housewives are able to buy their food at the RCAF Special Canteen at Montreal prices. Many are the families

*The above article expresses the personal views of the author and are not necessarily those of the Royal Canadian Air Force.

who, when their 2 year tour of duty is up, really hate to leave the small "World" of Goose Bay.

No matter how hot the days, the nights were always pleasantly cool and very conducive to a good night's sleep. Their summer "per se" begins about the 31st of May and lasts until Aug. 15. At the beginning of this period, the sun sets about 10:00 P.M. and rises again around 2:30 A.M., but the nights gradually lengthen as the summer wears on. During this summer period it is quite warm enough to wear summer-uniform shirt and trousers and even go bathing in the lake. But by the 15th of August winter uniforms appear, and snow flurries make a scattered appearance in early September.

The RCAF Hospital was responsible for the health and welfare of all Canadian personnel including R.C.A.F. and D.O.T. personnel; their wives and children (both born and expected); and also the many R.C.A.F. civilian employees who staffed the telephone switchboards, the typewriters, and the laundry. Although only classed as an 18 bed—4 bassinette Hospital, it does the turnover of a 50 bed hospital—but a new one is on its way. Presiding over our internship were two M.D.'s—the Senior Medical Officer—Squadron Leader N. St. G. Wade M.D. and a Medical Officer Flight Lieutenant E. G. Ramsay M.D. (For the non-Air Force types, these ranks are the equivalent of Major and Captain respectively).

Seven vivacious Registered Nurses composed our Nursing Staff of:— a Matron, 4 General nurses, a Public Health nurse and an Operating-Room nurse. The remainder of the staff was made up of 5 Medical Assistants, a very capable Lab technician, an obliging X-Ray technician, a patient and always helpful Pharmacist, and the efficient Orderly Room clerks.

Our schedule was full and interesting. Every morning was Sick Parade: R.C.A.F. personnel 9:00 to 9:30 A.M. and civilians and dependents 9:30–10:30 A.M. This of course was being very optimistic, for we seldom finished before 11:30 A.M. Aside from the usual coughs, colds, and athletes feet, we dealt with Infective Hepatitis, Pyelonephritis, Penicillin reactions, infected Black Fly bites, Measles, and neurotic women. One thing I learned very well and that was to get rid of the mother when treating the child. I had a mother faint in the treatment room while I was cleaning and dressing her 4-year-old's lacerated knee who incidentally uttered not a sound of complaint. Monday afternoon was devoted to physical examinations of new civilian employees. This included chest X-Rays, and blood WR; as well as the physicals. Tuesday afternoon saw all the expectant wives at Ante-Natal clinic (our SMO was obviously from England). It was indeed a busy afternoon for the two M.D.'s, for the begetting of children at Goose Bay received a high priority. Then Well-Baby clinic was conducted on Wednesday afternoon. This was held at the school with the Public Health nurse, a volunteer nurse-turned-housewife, the M.O., and the 2 senior medical students taking care of the details. The purpose of this "Monster-Clinic" as it was affectionately called, was to examine the babies for congenital defects and poor hygiene, and to start them off on their TABTD inoculations and smallpox vaccinations. Schick tests were periodically carried out

as well. In preparation for this afternoon it was necessary for each of us to take the following prescription:

Rx Sleep—Tuesday night 10 hrs.
Exertion—Wednesday morn. nil
Benzedrine 10 mg.
Sig:—follow as above and take Benzedrine 1 hr. before "Clinic" time.

Even with this, it was all we could do to drag our weary bones back to the Mess at 5:00 P.M. These protesting little bundles were the chubbiest and most energetic of any on the whole continent. One Wednesday I was examining a sweet young thing of 9 months and hoping to prevent her from crying I handed her my percussion hammer. As a result I nursed a bump on the forehead for 2 weeks. After that they played with tongue depressors and liked it!

Thursday afternoon was for routine D & C's on post-partums, for those innumerable "left to tomorrow" jobs, and for Bocknek's Wart Clinic where finger-blocks were practised with great zest. Post natal clinic was held Friday afternoon and it was indeed a pleasure to see all the newly-trimmed matrons proudly waiting for the SMO's words of advice on exercise, and diets.

Even though this schedule existed, babies paid absolutely no attention and had the worst habit of arriving at all hours of the night. If the Student M.O.'s were not at the Hospital when a birth was imminent, we were located and stood by to assist whenever necessary. I am sure one primipara in particular will long remember my hands as the site for her digging nails, for I still have one cherished scar to remind me. The great majority of births were simple and very quick with the patient kept semi-conscious and co-operative by the use of "Trilene."

Then, of course, there were the "party types" who insisted on meeting with immoveable objects between 1:00 and 6:00 A.M., and required suturing. I recall my first "sewing job" very vividly. One Saturday morning, the SMO had given me a demonstration of, and a tutorial on suturing, after which I felt quite sure that now I could handle such emergency matters. That night the SMO and I were on "call" and at 1:30 A.M. I was summoned to the Hospital. Awaiting me was an airman with a 2″ forehead gash, and escorted by 2 Service Police. But the self-assurance which I had felt that morning disappeared and I immediately appealed to the SMO who had by that time arrived. What would you do if a man whom you greatly admired and respected turned to you and said—"surely you can handle this yourself?" I'm pretty sure you'd try to justify his faith in you and that's exactly what I did. Since the patient was already "self-anaesthetized" there was no need for a local. I scrubbed my shaking hands, put on the rubber gloves and trying hard to act as though I had done this before, I put in three 6-0 Dermalon sutures. When it was dressed, I took a long drink of water and sat down. No sooner had I done this, when two more Service Police came in with another "anaesthetized" individual. As it turned out, he was a friend of the first patient and had felt quite annoyed when the S.P.'s took away his companion. So he too was taken into custody. But this was a greater insult, so he promptly revolted and smashed his fist through a one-inch shatterproof cell window. You can imagine the condition

of his hand. From his wrist distally along the thenar palmar-furrow was a 4″ gusher. By this time I felt more capable to the task, for had I not successfully completed my first suture case? At first I thought he had cut through his superficial palmar arterial arch and that I would have to start looking for ends to clamp, but my fears were unfounded for I was able to arrest the bleeding with elevation of his arm and pressure on his radial artery at the wrist. Then things came to my mind: damaged Recurrent branch of Median nerve; fractured hand; glass in the wound. But as long as the bleeding had stopped, I could carry on systematically. Thumb action was present, and sensory nerve intact after a good jab, for his senses were well dulled. X-Rays were taken and were developed as negative while I continued my "operation No. 2." Slight adduction of the thumb to take tension of the suture line; careful alignment of the edges; 8, 6-0 Dermalon sutures; vaseline-gauze dressing and 300,000 units of Penicillin I.M. completed my activities on him. Is there any wonder I remember that night? When the stitches were removed and showed the faintest of scars and no contractures I felt for the first time that inner self-satisfaction of finally being able to do something in Medicine.

Our Medical wards were composed of the admissions from Sick Parade as well as cases of myocardial infarction, angina pectoris, and gastric ulcers. It was the job of the Medical Students to admit, examine, provisionally diagnose and prescribe for them, under the supervision of the M.O. One case in particular will always remain with me. One Saturday morning in early September a well-built 165 lb. 48 yr. old R.C.A.F. Corporal came in to Sick Parade. In summary his chief complaint was sore throat and chills for past 2 days, and tender gums. Remainder of history was negative. On examination his tonsils were studded with 4 small white follicles, his throat and gums slightly inflamed, a temp. of $100.8/$, a small herpes labialis, slightly enlarged, non-tender tonsillar lymph nodes Hb 85% and WBC 12,000. Rest of Physical yielded absolutely nothing more. The Dentist was called to look at his gums and gave his opinion as a mild Vincent's. Provisional diagnosis was made of Follicular tonsillitis with mild Vincents', and patient was admitted to hospital while protesting rather vigorously that all he needed was some aspirins. However he remained, and was put on Penicillin 300,000 units daily; Mandl's paint q.4.h.; APC and Codeine grs. 1/8-tabs 2, q-4.h; Bacitracin ointment to Herpes; and arsphenamine cpd. mouth wash for Vincents. After 3 days of treatment, only one follicle remained on his tonsils, his gums were not as tender but just as inflamed, his Herpes was the same as before, his Hb was 70% and his WBC was 15,000. A look at his chart showed a Remittent type of fever, —and then the M.O. suggested a blood smear. One look confirmed his suspicions —the slide was packed with myeloblasts! But our patient still showed no more physical signs and felt as strong and energetic as usual. However, the blood told the story, and the "Tonsillitis with Vincents" was now diagnosed as Acute Myelogenous Leukemia.

He was sent to Sunnybrook Military Hospital so he could be near his family here in Toronto, and was put on Penicillin and Streptomycin therapy. His WBC rose to 85,000, then to 105,000 and his Hb. dropped to 53% then to 42%. An

experimental drug G.T. 41 was tried, he was given blood, but his WBC rose suddenly to 165,000, his Hb dropped to 38% and he died 7 weeks after his first symptoms. But it was not until 10 days after I saw him that he began to feel acutely ill with malaise, cutaneous hemorrhages, and palpable spleen.

At times we even had Eskimo patients in the Hospital, from Northern Labrador and Baffin Island—with tuberculosis (meningeal, pulmonary, or miliary); fractures; mumps; rheumatic carditis; pneumonia, corneal ulceration and periostitis of the mandible.

I think that everyone will agree with me as to its being one of the busiest 18-bed hospitals in the world, and that the Nursing Staff deserves much credit for the efficient management of such a cross-section of diseases and people.

The R.C.A.F. at Goose does all in its power to evacuate seriously ill Eskimoes from Northern Labrador and Baffin Island and I was sent on 2 of these Air Evacuation missions. One was to Hebron, 400 miles north of Goose on the Labrador coast, and the other to Fort Chimo and Frobisher Bay, 400 and 700 miles north respectively.

A 4 year old boy who had been to Montreal for treatment was to be returned to his Moravian Missionary parents at Hebron. For two weeks he lived at the Hospital and became thoroughly spoiled. If he could not be located outside, for dinner, he could always be found in either the Nurse's quarters or the Airwomen's quarters visiting the girls. It was truly a privilege to go looking for little Ian Grubb! It was at this time that we received a signal informing us of a 6 year-old Eskimo boy with a fractured femur waiting at Hebron for transfer to our hospital. So one July morning little Ian Grubb, the O.R. nurse, and myself took off for Hebron in a PBY-4 flying boat. For the first time I saw ice-bergs and was amazed at the different colours they reflect from the water. From the air one can see just how treacherous they are, for their bases project far out under-water. With little "Grubby" munching oranges to occupy him, the trip was quite quiet and enjoyable. We exchanged patients at Hebron and landed back at Goose with "Elias" our fractured femur, 13 hours after our initial take-off. The Eskimo boy had fallen and fractured the upper 1/3 of his femur 5 days before we got to him and traction proved useless. When X-Rays showed callus formation, an open reduction was performed and I understand that he is now walking about the Hospital up at Goose, no doubt badly spoiled.

The other trip was to Fort Chimo to return 3 Eskimo patients and then on for a one-day Medical Inspection of the Eskimo village just outside the R.C.A.F. Detachment at Frobisher Bay. In the summer months the Eskimoes live in skin tents and in the winter in packing-case shacks. Their main sustenance is fish, seal and bear; and Coca-cola, chocolates and cigarettes in return for emptying oil-drums for the Air Force. It is not unusual to see 11 year old girls smoking cigarettes like veterans. Although these people live in absolute and complete poverty, they are the happiest, most co-operative and most appreciative people one could ever hope to meet. No matter how great their pain, they always had a smile for you. Although I was not able to witness any of their mechanical feats, the boys at Frobisher told me that any of the Eskimo lads could take an ordinary type of engine completely apart

and put it back together in working condition without ever having seen it done. Can you imagine what they could do with technical training? A very queer thing struck me at Frobisher, every tent had a Westclox America alarm clock keeping correct time!

Besides T.B., measles is an Eskimo killer. During an epidemic at Frobisher, the mass inoculation of .1 ml. of gamma-globulin /lb. body wt. worked wonders in cutting mortality and severity of the disease.

In regard to social life the U.S.A.F. had their Officer's club of which all R.C.A.F. Officers were honourary members. This club was modelled after American nightclubs with a lobby; a barroom; and a main ballroom set up cabaret style with dim lights and mirrored pillars. Our own Officer's Mess was unbelievably luxuriously built centre-plan. One side contained a dining-room complete with tables for six with waitress service, and the other side contained the Games-room with billiards and ping-pong; a huge ballroom; and also a beautiful Pine Room panelled completely in varnished wood and furnished with plenty of soft chesterfields. From the Pine Room one could relax, and look through the 4 huge picture windows at the Bay. It was a beautiful picture at night with the riding lights of the ocean freighters in the Bay and the coloured Northern lights in the sky. There was always something in progress at one or all of these clubs, either a Bingo, a Games night, a Stag-night, a theatre night, or a dance. For these dances we had dance bands of either Canadian or American personnel—and they were good. Goose Bay also had its share of Formal dances too, without corsages. Two theatres, one Canadian and one American showed the latest films—2 shows nightly, and 3 on Saturday and Sunday, for only 25c. per person. And of course, one never tired of going for long walks under those phenomenal Northern Lights, then for coffee in the Nurse's quarters.

As the weather grew colder and snow flakes began to fall, we three realized that all too soon our stay at Goose was coming to a close. After 3½ months we reluctantly bade goodbye to its inhabitants and to "our Hospital," taking back with us, many wonderful memories and experiences—(not soon to be forgotten).

It is the policy of the RCAF University Reserve Training Plan to employ their Officers in an Air Force Branch and List which is complementary to their University Course. Following this plan, Medical Students in their Clinical years are listed as Med/MO's and as such, are employed in an Interning capacity at RCAF hospitals throughout the country.

If I were founding a university I would found first a smoking room; then when I had a little more money in hand I would found a dormitory; then after that, or more probably with it, a decent reading room and a library. After that if I still had more money that I couldn't use I would hire a professor and get some text books.

STEPHEN LEACOCK

CARCINOMA OF THE OESOPHAGUS

R. KIMOFF, 5T3

This is a disease of insidious onset, swift progression, and rapidly fatal termination. It has been estimated that from the onset of the disease to the beginning of symptoms is 5-6 months; from the onset of symptoms to the diagnosis another 5-6 months; and the average duration of life after diagnosis, 5 months (2). Hence early diagnosis is essential.

Anatomy

Thorough knowledge of anatomical relations is essential. A few points are worthy of note.

Grossly: intimate relationship of vital mediastinal structures makes early local spread simple and dangerous.

Blood supply of oesophagus is "shared" with neighbouring structures, hence in mobilizing any part, care *must* be exercised lest ischaemic death of a part be caused, particularly of the oesophagus.

Lymphatic drainage is both cephalad to nodes around the respiratory tree and caudad to nodes around the oesophagocardiac junction. There are wide communications with nodes draining the pleura, as well as intercommunications between oesophageal lymphatics proper. This leads to early, widespread dissemination and makes radical removal of all involved lymphatics hopeless.

Microscopically: Oesophagus has no serosal coat, and its muscle is not strong enough to hold sutures if any tension is exerted. This makes anastomosis more difficult than in the intestine whose serosa does hold sutures well. However, oesophageal mucosa and muscle hold sutures well.

Pathology

Incidence: Oesophageal carcinoma constitutes 5-7% of all malignant disease. It is commoner than benign oesophageal neoplasms. It occurs in males over fifty, but an age range of 28-81 years of age has been found.

Site: It occurs at normal points of narrowing—upper and lower ends and the point where the left bronchus crosses. (Some, however, question this belief.) The lesion may occur anywhere. In women, about half the cases occur at the upper end, related to post-cricoid cancer.

Predisposing Factors:

1. Poor teeth plus rapid eating plus alcohol—hence the disease is more common in men.
2. Plummer-Vinson syndrome (dysphagia, glossitis, hypochromic anaemia).
3. Trauma—such as lye burns. It is doubtful that this is a very important factor.

Gross: Single, but occasionally multiple lesions.

1. Ulcerative—commonest type; gives characteristic malignant ulcer.
2. Fungating or polypoid.
3. Diffuse.
4. Scirrhous.

The latter two are rare.

Microscopic: It is most often squamous cell in type, but columnar cell, glandular, keratinizing, and anaplastic types occur. Adenocarcinoma usually occurs at the lower end, (considered by some a submucosal extension of gastric carcinoma) but occasionally at the upper end also.

GRADES:

I. Grossly confined to oesophagus —*less* than 10% patients.
II. Direct spread to adjacent structures, but not extensive.
III. Mediastinal nodes involved.
IV. Distant metastases present.

About 75% patients present as grade III or IV.

SPREAD: Occurs less often with upper one-third than with lower one-third lesions. Upper one-third reach cervical, lower one-third, abdominal nodes.

1. By direct extension to adjacent structures. Microscopic spread is 1-4 cm. at least beyond gross extent of the lesion—this is important in resecting the lesion.

2. Lymphatic—regional nodes involved in most cases *early*.

3. Blood spread to liver, thyroid, ovaries, spleen, pancreas, pericardium, bone and brain occurs later.

COMPLICATIONS:

1. Peri-oesophageal suppuration from perforation, lymph node suppuration, or lymphatic spread of infection from tumor area (mediastinitis).

2. Haemorrhage—repeated minor or single severe fatal (erosion into aorta).

3. Respiratory:

1 Larynx—causes difficulty in phonation or laryngeal dyspnoea.

2 Ulceration into trachea or bronchi with fistula formation.

3 Lungs and pleura—infection: empyema, lung abscess.

4. Nerves: Recurrent laryngeal—vocal cord spasm from irritation, then paralysis.

Sympathetic trunk — Horner's syndrome.

Vagus—no symptoms; or causes dyspnoea, cough, vomiting.

Phrenic—hiccough, then diaphragmatic paralysis.

Intercostal—neuralgic thoracic pains.

5. Thyroid.

6. Oesophagus—obstruction, first to solids then to soft foods.

7. General—much emaciation.

DIAGNOSIS

On the basis of symptoms, signs, radiological and endoscopic examination, and oesophageal washing with examination for malignant cells. Thoracotomy is justified if all laboratory tests fail yet symptoms suggest neoplasm.

1. *Symptoms*

A. Early

1. "Indigestion"—earliest phase of dysphagia. To the patient it is a vague tightness or indigestion. Later, food may occasionally stick, then normal deglutition be present for several weeks before real dysphagia occurs.

	Squamous Cell			Adenocarcinoma
Initial Symptom	Upper 1/3 15 patients	Mid 1/3 32 patients	Lower 1/3 23 patients	 18 patients
Dysphagia	8	16	14	12
Regurgitation (often not early)	0	2	2	1
Throat discomfort	9	2	1	0
Substernal discomfort	0	5	2	3
Epigastric discomfort	0	5	2	3

2. Epigastric pain on swallowing, intermittent at first, then continuous.

3. Immediate belching on swallowing.

4. Throat discomfort (may be burning from oesophagitis).

5. Substernal discomfort—oppression, fullness, with colicky sensations on swallowing.

6. Regurgitation occasionally.

7. Excess saliva or mucus in the throat.

8. Anorexia, indigestion.

Carcinoma of the upper third was in this series diagnosed more readily purely from history and physical examination than carcinoma in other areas (4).

B. Late

1. Frank dysphagia from spasm of wall and obstruction by tumor, usually localizes the tumor. Dysphagia with solids, then liquids. Temporary improvement may occur from sloughing of part of the mass.

2. Pain from local muscle distension above the lesion. It is substernal or at the back of the neck, and is segmental. Pain from perioesophageal inflammation due to penetrating growth or invasion of spine or adjacent oesophageal viscera, is steady boring, aching. Earache may occur from growth in hypopharynx.

3. Vomiting of unchanged food.

4. Excess salivation with hypertrophy of salivary glands. Glands return to normal size, when swallowing re-established.

5. Bringing up moderate amounts of blood, or sudden profuse haemorrhage and death.

6. Cough.

7. Hiccough.

8. Hoarseness due to recurrent nerve paralysis.

9. Anorexia, decreased weight and strength, pallor, anaemia, cachexia, thirst from dehydration.

From the onset of the disease to the first symptom is 5-6 months. From the first symptom to the diagnosis is 5-6 months. The average duration of life after diagnosis is 5 months (2).

2. *Physical Examination*

This is not usually of much value. It may discover the dehydrated or cachectic patient; it may discover a unilateral bulge on one side of the neck which could be a dilated oesophagus, tumor mass or group of enlarged lymph nodes; it may disclose enlarged supraclavicular or posterior triangle nodes; or finally, a pouch or tumor anteriorly below the cricoid.

3. *X-Ray*

A flat plate and barium swallow should be done, coupled with fluoroscopic observation of barium swallowed, noting here the very beginning and very end of the oesophagus. Both these regions are easily missed on an X-ray plate since barium is not always caught at these points in the plate. Look for:

a. Local irregular contour of the lumen.

b. Narrowed lumen.

c. Destruction of normal mucosal folds. At times, a so-called "fingerprint" deformity occurs with a polypoid lesion.

d. The constriction of the lumen may be smooth, suggesting a benign lesion.

Remember: A negative X-ray examination does not mean that there is no lesion. Six out of 88 false negatives were reported in one series (4).

4. *Endoscopy*

1 *Oesophagoscopy*

Always follow X-ray by oesophagoscopy. If a lesion is seen, consider it carcinoma until proven otherwise. This gives an opportunity for biopsy, for seeing the extent of the lesion and determining the presence or absence of fistulae.

2 *Laryngoscopy*

This is done to evaluate any associated nerve lesion, to exclude a lesion in the larynx or pharynx, and to look for any postcricoid carcinoma.

3 *Bronchoscopy*

This is done if there is any suggestion of bronchial tree involvement, and may be done to exclude such spread which is not giving symptoms when attempting to determine the operability of the patient.

5. *Biopsy*

This is done via oesophagoscope in the usual manner, or by passing an instrument beyond the lesion and taking a retrograde biopsy. A negative biopsy should be repeated. In minimal malignant lesions a positive diagnosis is sometimes missed. Care is necessary to avoid creating a perforation while taking the biopsy sample.

6. *Abnormal Cytology* (5, 6)

A double lumen tube with a balloon on the end is passed until the balloon is in the stomach. It is then inflated and pulled snugly against the cardiac opening of the oesophagus. About 45 c.c. of saline are injected into the oesophagus and removed. This is repeated several times, the fluid finally withdrawn, centrifuged and the sediment fixed and sectioned, then examined for malignant cells. A so-called carcinoma *in situ* which was missed by biopsy was found by this method.

7. *Exploratory Thoracotomy*

If history, physical examination and X-ray are positive, but biopsy and oesophagoscopy are negative, a thoracotomy is justified.

Differential Diagnosis

1. *Extrinsic Compression of the Oesophagus*
   1 In the neck:
      —thyroid
      —enlarged lymph nodes
      —nerve tumors
   2 In the mediastinum:
      —retrosternal goitre
      —aneurysm of thoracic aorta
      —lymph node enlargement
      —inflammatory lesions such as chronic mediastinitis or peri-oesophageal abscess
   3 In the abdomen:
      —gastric carcinoma
      —subphrenic abscess
2. *In the Oesophagus Itself*
      —spasm
      —cardiospasm
      —diverticulum
      —benign polypi
      —ulcers:
      simple
      specific—typhoid, diphtheria, granulomata
      —inflammatory stricture
      —hiatus hernia

Never be satisfied with a diagnosis of cardiospasm until carcinoma is ruled out, and when ruled out, follow the patient regularly, since carcinoma develops more readily in this patient.

Treatment

Evaluation of the Patient Regarding Operability

1. Age—not as important as patient's general condition, especially that of his cardio-vascular system.
2. Cervical node involvement.
3. Metastases to lungs or pelvis (seen on X-ray) or to liver.
4. Endoscopy to determine invasion of bronchi, trachea or larynx.
5. Extent of lesion itself as determined by X-ray.
6. Presence of intense boring back pain.

Any signs of spread or poor cardio-vascular system preclude possibility of operative cure. In some cases, palliative treatment may be attempted.

Pre-Operative Preparation

1. Improve the general condition of the patient by feeding high protein fluids. If obstruction is complete, an ileostomy or gastrostomy might be used.
2. Oral hygiene cared for; any dental work necessary is carried out.
3. Blood transfusion if needed, or intravenous substances to try to achieve proper electrolyte balance.
4. Penicillin, 50,000 units q.3.h. 48 hours before operation.
5. Lavage with half strength Dakin's solution b.i.d. for 3-4 days pre-operatively if obstruction is complete or almost so.

Operative Procedures

Treatment which does not restore swallowing is inadequate. Gastrostomy, once much used, has now been abandoned (7). (1) It does not prolong the life of the patient with inoperable carcinoma. (2) It adds to the patient's misery by excoriation around the opening, wound infection, blocking of tubes, and repeated painful dressings. (3) The patient still salivates when fed through the gastrostomy and is unable to swallow his saliva. Carcinoma of the oesophagus is rarely cured by operation; hence one should strive for palliation (8).

Carcinoma of lower quarter:

If resectable
—remove tumor, then perform oesophagogastrostomy.

If inoperable
—form an intrathoracic shunt with a Roux-Y jejunal loop.

Carcinoma of midoesophagus:

If resectable
—remove tumor, then do an oesophagogastrostomy.
—remove tumor, then do an antethoracic oesophagoplasty.
—remove tumor, then do a plastic tube reconstruction.
In this last, fibrin is laid down around the tube, epithelium grows in from each end to line the fibrin, and the tube is passed spontaneously in time.

If non-resectable
—antethoracic oesophagoplasty with irradiation should be done.
—silver tube through the narrowed area, plus irradiation.

Carcinoma near thorax apex:

Antethoracic oesophagoplasty with or without resection or irradiation may be done. In carcinoma of the cervical oesophagus, it is possible to remove the larynx, upper oesophagus and trachea and form a new upper oesophagus by infolding a flap of skin, or by inserting a tantalum mesh across the gap from pharynx to oesophagus and covering it with skin graft.

Debilitated patient: palliation.

—Bouginage
—Tube through narrowed lumen
—Irradiation: radium bougie or deep X-ray gives rapid relief of dysphagia.

Post-Operative Care (for thoracic or thoracoabdominal approach) (9)

The first few post-operative days are very important. If the regimen is carefully explained and clearly understood *pre-operatively*, there will be more co-operation when it is needed.

1. Water trap drain—remove in 4-5 days if no fluid in chest.

2. Daily chest examination.

3. X-ray of chest on first, third and seventh post-operative days.

4. Aspirate fluid if dyspnoea occurs or if more than one-third of the chest is full of fluid.

5. Stir up regimen:
—6-10 deep breaths every half hour, or CO_2 plus air to cause deep breathing.
—frequent turning from side to side.
—coughing.
—early mobilization: on side of bed on second post-operative day, in a chair on third day.

6. Tracheo-bronchial toilet: aspirate at once secretions in the bronchial tree when they appear, via endotracheal tube with topical anaesthesia or carcinoma bronchoscope.

7. Suction with a Rawson-Abott tube, the distal lumen in the duodenum or jejunum (if Roux-Y anastomosis done) for feeding, and the proximal lumen in the stomach to prevent distension due to gastric atony caused by vagus section.

8. Oxygen give at slightest sign of hypoxia.

9. Sedatives at minimum to maintain cough reflex.

10. Antibiotics:
Penicillin given intramuscularly into pleural cavity, and nasal inhalation pre-operatively.
Streptomycin and sulphonamides as indicated.

11. Fluid and food.
1 Intravenous fluids. Give saline only if patient is vomiting and losing salt.
2 Blood transfusion. Amount is governed by the amount of blood draining from the chest and by indications of anaemia.
3 Drip feeding via tube. Begin on protein, carbohydrated, vitamins C, B, K on second or third post-operative day. Avoid food which curdles. Discontinue if leakage occurs at anastomosis (food comes out chest drain).

Post-Operative Complications

1. Leakage at anastomosis or formation of aortoesophagogastric fistula.
2. Strictures.
3. Atelectasis.
4. Mediastinitis.

Other complications which follow surgery or a long stay in bed may also occur.

Radiation Therapy

If a carcinoma mass does not exceed 70-100 c.c. in volume, X-ray cure can usually be accomplished. A lesion whose visible extent on X-ray is greater than 5.1 cm. in length cannot usually be

cured by radiation. Lymph node secondaries are usually radio-resistant. Oesophageal carcinoma is highly malignant and moderately radio-sensitive. There is some disagreement as to the usefulness of radiation in oesophageal carcinoma. Some report complete disappearance after radiation or after insertion of a silver tube to re-establish deglutition, followed by radiation. Some use radiation and nitrogen mustard together.

Methods:

1. Insert radon seeds into the tumor via an oesophagoscope or by thoracotomy.
2. Radium bougie.
   1. and 2. do not give an even, adequate dose over the whole tumor.
3. External radiation.

Effects of high voltage irradiation:

1. Relieves dysphagia.
2. May prolong life.
3. Gives good results in tumors of the upper one-third.

Prognosis

Prognosis is uniformly gloomy when the 5 year survival rate is considered, but patients whose deglutition has been restored lead a fairly comfortable life until their demise. Opinions differ as to whether there is any different outlook for the person with squamous cell carcinoma as compared with the one with adenocarcinoma. Most report few, if any, 5 year survivals. Sweet, however, reports the following (10).

Five year survival:

lower oesophagus—17.5%
midoesophagus—4%

There is no difference between squamous and adenocarcinoma survival rate.

Lymph nodes: negative—40%
positive—13.5%

Others have found that if the anastomosis is (a) proximal to the aortic arch, mortality is 61%, and if (b) distal to the aortic arch, mortality rate is 10%.

In conclusion it is stressed that one must remember that any degree of dysphagia, transient or progressive, should be considered of carcinomatous origin until proved otherwise.

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EDITORIAL

THE NEW MEDICAL CREST

After many years of deliberation, the Faculty of Medicine, of the University of Toronto is the proud possessor of a Crest which is distinctly its own, and one which will unify the six years in the Faculty under a single design.

The idea of having a solitary pattern which would be satisfactory to all years in Medicine was initiated by the Medical Society two years ago, and several designs were considered briefly then rejected. After many conferences with Mr. Alexander Scott Carter R.C.A., an authority on Heraldry, a striking and original Coat of Arms was designed. It has now been in use for several months on official Faculty stationery, and the Medical Journal, and is beginning to appear on blazers around the campus.

The *escutcheon* or shield is the basic portion of any authentic Coat of Arms. Our shield is white in color, pointed at its lower end, and cut transversely at its upper end. A large serrated black cross divides it vertically and horizontally into four quarters. At the centre of the cross a large *fusil*, an elongated diamond, is situated which in turn has the staff of Aesculapius superimposed on it in gules. Between the points of the

fusil and each of the four ends of the large cross is a *plate*, a round pill-like structure.

In each of the four areas formed by the angle of the two arms of the cross are several symbols, the *crux ansata* which were regarded as a symbol of life in ancient Egypt, and as a symbol of the sun in Gaul.

An ornamental scrollwork, the *mantling* appears above the shield in the form of sable and silver interwined bands. The mantling originally represented the scarf worn around the body beneath the coat of mail.

The *crest* which was originally a special mark of honor is placed above the shield like a plume. In this case the crest is an oak tree, fructed proper (i.e. bearing fruit) and depicted in its natural color.

The *scroll* is placed beneath the escutcheon and bears a war cry or motto. The motto chosen for the Coat of Arms of the Faculty of Medicine, University of Toronto, may be translated quite appropriately as: "I treat him, God cures him."

F.P.C.

THE CHOICE IS OURS

In the spirit of the New Year, while we are still anxiously clinging to a few unbroken resolutions and our ideals are high, a word about the plight of the Journal might be worth a few moments meditation.

Each successive Journal staff has faced a problem which is extremely unique—that of producing an undergraduate publication for distribution chiefly among students, but without receiving the support of student contributions. This peculiar situation has resulted every year in requests for student articles, sometimes in repeated subtle tones, sometimes in loud pleas, but always in desperation.

Ironically enough, the greatest response has always been from people who have been associated with other organizations; Daffydil, the Osler Society, etc., who would ordinarily seem to be the most occupied and have less time to write for the Journal. Yet these students do find time somehow to apply themselves more liberally to their environment, even at the risk of being accused of having only social inclinations, and in some instances of "stealing the show" from less concerned members of the undergraduate group.

The fact still remains that organizations within the Faculty exist not for the benefit of a few interested persons, but for the whole Faculty unit, and therefore should receive more support than they are now getting.

We have then a choice to make. We can terminate the existence of any organized body within the Faculty, if it is no longer serving the interests of the majority of the undergraduates, or we can allow it to die a slow, painful death, through lack of cooperation and interest. Such a choice at least, is effortless.

No bubble is so iridescent or floats longer than that blown by the successful teacher.
Sir William Osler

SIR FREDERICK BANTING

J. F. MUSTARD, 5T3*

"There is a tide in the affairs of men
Which, taken at the flood, leads on
to fortune."

The first thirty years of Banting's life, while he was pitting himself against the arbitrary standards of his fellow-men in his educational training, had little to suggest that this average student would answer a problem that had bewildered scientists and clinicians. As the days progressed from his birth in 1891, it became evident that he was a serious student not inclined to be jolly. Being the youngest of five children he was seldom called upon to interrupt his education for work on the farm, and he was, as well, his mother's favourite. This latter fact has led some persons with a psychoanalytical tendency to claim this as the basis of a mother fixation complex that explains some of his behaviour in adult life.

As he neared the completion of his high school education at Alliston which was near the family farm, his interest in medicine grew, but his family preferred that he go into the Methodist Church. Consequently in 1911 he enrolled in Victoria College at the University of Toronto. Here, as in his earlier education, he found great difficulty in subjects that required memorization, stumbling badly with Latin and French. His mind was not adapted to comprehend a diversity of subjects, the majority of which required memorization. Instead, it was suited to a concentrated effort on a definite subject in order to obtain a desired result. He would not make shallow assimilations of knowledge to give back to his examiners—but rather, he slowly went over all that he was interested in and thought deeply about it.

He left Victoria College at Easter and returned to college in the fall, this time to enroll in the Medical School. He was a member of the class of 1917. The students of this class soon found themselves faced by the question of whether to complete their course or join the army. Although Banting was tempted to leave school to join the army, he was persuaded to complete his course and thus sublimated the energy of his own wishes by being a drill sergeant in the C.O.T.C. He was not noted as a scholar, for he was of grade C standing, but he did have some reputation as a rugby football player on the inter-year and inter-faculty teams. The diligence and perseverance that were to mark his later work were shown in his habit of re-reading each text thoroughly several times and in the faithful, persistent manner with which he carried out his laboratory work, especially in physiology, where he would even eat his lunch in the laboratory rather than leave an experiment.

Banting graduated from Medical School on December 4, 1916, and joined the army the next day. He was soon sent overseas where he joined a special hospital at Ramsgate. Banting in his undergraduate years had found Dr. C. L. Starr, then Chief Surgeon of the Hospital for Sick Children, his most inspiring teacher. This influence caused him to

*From an address to the Osler Society, September 1952.

favour orthopaedic surgery. While at Ramsgate he found that with such men as Dr. W. E. Gallie on the staff he could further study his interest. He would spend his off hours collecting china and studying texts in surgery. The latter, he hoped, would prepare him to attain his degree in surgery soon after the war. With the actuality of real fighting so close, he found himself anxious to see battle, and later in 1917 he was sent to France with the Thirteenth Field Ambulance. He was a good battlefield surgeon, abiding by his motto "Never leave a job half done."

An 18-pounder field piece was moved into the yard of their dressing station one day, and soon drew the enemy's fire with the result that there were several casualties. Among them was Banting who received a deep wound in his right arm severing his interosseous artery. Major Palmer ordered him to the Central Clearing Station. Palmer however had to go forward to set up another post, and Banting ignored the orders as he was the only medical officer left. When Palmer returned seventeen hours later, he found Banting haggard, exhausted and weak, still tending the heavy flow of casualties. This time he did get him away and Banting was sent to England to recover. For Banting's strength and fortitude after several days of difficult and trying work he was awarded the Military Cross.

The war ended about the same time as he recovered the use of his arm. He soon returned to Canada, where he joined the interne staff of the Hospital for Sick Children under C. L. Starr. He spent a year here furthering his training in orthopaedics. As July 1920 came near, he and a fellow classmate, Dr. W. P. Tew (Professor of Obstetrics and Gynaecology at the University of Western Ontario) made plans to go to London to set up practice.

Banting's office in London only collected cobwebs. Rather than allow his mind to become as badly off, and also to keep himself from becoming an indigent, he took a position demonstrating in Anatomy, and working in Physiology at Western University. This concludes the first part of his life—the preparation.

II

"Pursue, keep up with, circle around and round your life, as a dog does his master's chaise. Do what you love. Know your own bone; gnaw it, bury it, unearth it, and gnaw it still."—THOREAU

The second part commenced on October 30, 1920, when he took home the November, 1920 issue of Surgery, Gynaecology and Obstetrics to read an article entitled "The Relation of the Islets of Langerhans to Diabetes with special reference to cases of Pancreatic Lithiasis," by Dr. Moses Barron. He was to talk to his students the next day on the functions of the pancreas. At 9.00 p.m. he telephoned Dr. Tew and asked him to come over and discuss the paper, especially the paragraph regarding the experimental ligation of the pancreatic ducts. Several hours after Dr. Tew had returned home, he wrote in his note-book, "Tie off pancreas ducts of dogs. Wait six or eight weeks. Remove and extract."

This idea was not new, but no one else had surmounted the technical problems, and their work was lost in the maze of material on diabetes and carbohydrate metabolism. Here, Banting's lack of information in detail prevented him from becoming too confused, and allowed him to see his idea clearly.

The officials at the University of Western Ontario felt that they could do little to help him with his idea, but they suggested that he see Dr. MacLeod in Toronto who was an authority on carbohydrate metabolism. Banting came to see the Professor of Physiology at Toronto, presented his case and found MacLeod unfavourable to his idea. Banting's stubborn nature refused to give in, so the next day he returned to MacLeod's office and restated his argument. Either his clarity, his determination, or both, persuaded the Professor to give him a small room, ten dogs, and eight weeks to prove himself.

Banting returned to London and finished his appointment at the University of Western Ontario. In May when Banting returned to Toronto, Mr. Best and Mr. Noble were appointed to assist him. Mr. Best commenced work with Banting immediately, but Mr. Noble did not participate in this early work. They worked feverishly, thinking of the eight weeks in which the work must be done. Banting's ability as a surgeon helped him greatly in depancreatizing the dogs and ligating the ducts which had to be under the right tension to get the desired result.

On July 27, 1921, a depancreatized dog with the signs of hyperglycemia and a duct tied dog with necrotic acinar glands and relatively intact islet cells were ready. They made the extract from the ligated pancreas and injected it into the depancreatized dog. The blood sugar level of the dog commenced to drop. To them it was convincing, but they knew that before others would believe it they must exclude all possible causes of a false result. When Professor MacLeod returned from Europe and saw their results, he found that of his many objections, only a few were not answered.

With the reality of the hormone now proven, the next problem was how to produce enough purified material so that it could be used in humans. Banting attempted to destroy the enzyme glandular areas by stimulating them with secretin and the vagus nerve until they were exhausted, at which time he would extract the intact islet tissue. Although this method worked and saved them the necessity of having to ligate the pancreatic duct, it did not greatly increase the supply of the hormone which was called isletin at this time.

Banting and Best knew from the work of others that the pancreas of newborn animals had more islet cells in relation to the whole pancreatic gland than in the adult. When they concluded that a foetus in the first third of pregnancy would have the maximum amount of the internal secretion, Banting's knowledge that most cattle are bred before sale directed them to the city abattoir from whence they returned with the pancreases of nine foetal calves. Although they now had a supply of insulin, it was only enough to allow them further laboratory research. It was still necessary to try to make an extract of the whole gland.

Early in August, 1921, they had attempted to extract insulin from the whole gland. When they did manage to prepare an extract, they found that they were unable to repeat it. Professor Henderson of the Department of Pharmacology, who had given Banting a position as demonstrator in his department to allow him an existence better than starvation, again came to the rescue. This time he pointed out how they could retrace the method of extraction which had been successful. The problem of purifying this extract was solved by Dr.

Collip (Dean of the University of Western Ontario Medical School), and the method of production and refinement by Best, with Fitzgerald, Defries and Scott at the Connaught Laboratories.

On January 11, 1922, in the Toronto General Hospital, Mr. Leonard Thompson became the first human to be treated with insulin. The hormone had to be tested clinically and further refinements made, but now it was proven beyond all doubt that the islet cells of the pancreas secrete insulin and that this hormone was a great aid in the treatment of diabetic patients.

The clinical application at the Toronto General Hospital was executed mainly by Drs. W. R. Campbell and R. R. Fletcher, with Banting as an outside advisor. Here was one of Banting's difficult problems—he was not accepted by the physiologists as a true scientist, and the clinicians did not regard him as a clinician. He was merely the man who had answered a difficult problem in physiology that allowed clinicians to turn what had been a mainly uncontrollable disease into one that could be controlled. Banting was disgruntled by this, and some observers claim that he was not mature in this situation. He was certainly a stubborn, forceful, impatient but generous man. Another difficulty arose when MacLeod, in the tradition of the old German schools of science, announced as head of his department, the discovery of insulin. This caused the world to believe that MacLeod had discovered insulin. Banting was so upset by this that he held a personal grudge against MacLeod for years after.

The actual contribution of all the members is difficult to assess. Professor MacLeod gave the laboratory facilities, the assistants Best and Collip, help on technical problems, and his prestige. Banting contributed the duct tied gland (which allowed the conclusive proof of the production of insulin in the islet cells of the pancreas), the non acinous foetal gland, the secretin exhausted gland, his determination and operating skill. Banting assigned Best equal credit in the discovery. Dr. Collip, who was greatly responsible for the purification of the extract, denies having really contributed anything.

The Eli Lilly Company offered its resources to help in the production of insulin when the group concerned thought it would be prudent. It was mainly through Dr. Clowes of this company that insulin was so sensibly and widely distributed for clinical use in so short a time. This led to very quick recognition of the work by the Nobel Prize Committee.

The process developed in Toronto was patented by Banting, Best, and Collip, but assigned to the Board of Governors of the University of Toronto. The process was then given away for the use of the rest of the world, the patent preventing exploitation and unauthorized manufacture of the drug.

III

"Fame comes to those who are looking elsewhere."

We can now enter into the third stage of his career—that of the celebrity. People from all over the world came to see the man who had found a way of helping to fight their disease. In contrast to his initial start in London, Banting was now forced to open an office on Bloor Street for consultation. He was wanted as a speaker at banquets and other elaborate functions. He had great difficulty in speaking to large gatherings,

and as well hated the social group, so that he soon restricted his engagements.

Banting did not capitalize in a material way on his discovery. The only rewards obtained were the heartfelt thanks of diabetics and the generous gifts of a grateful world. His awards were:

1922: The Starr Gold Medal
George Armstrong Peters Prize
1923: Reeve Prize
Charles Mickle Fellowship
Nobel Prize in Medicine
John Scott Medal (Philadelphia)
1924: Rosenberger Gold Medal (Chicago)
1927: Cameron Prize (Edinburgh)
1931: Flavelle Prize (Royal Society of Canada)
1934: Apothecaries Gold Medal (London)
1936: F. N. G. Starr Gold Medal of the Canadian Medical Association

In 1934 he was created Knight Commander of the Civil Division of the Order of the British Empire. In 1935 he was elected a fellow of the Royal Society of London.

The Nobel Prize when awarded stirred up his old grudge against MacLeod, as it was awarded to MacLeod and Banting: Best had been ignored. He suppressed his feelings and accepted the award, sharing his half of the $40,000 with Best. MacLeod divided his share with Collip, thus making it an equal recognition to all who had played a major part.

The Dominion Government in 1923 recognized Banting's work and granted him an annuity of $7,500. The Ontario Government made a grant of $10,000 annually for a Banting and Best Research Fund, part of which was to support a chair of medical research. Banting was made Professor of Medical Research in 1923, the first in the history of the University of Toronto. Sir Robert Falconer asked Sir William Mulock to see if he could organize a campaign to raise $500,000 or more to establish a Banting Research Foundation. This was readily done, and by the time of Banting's death nearly two hundred workers had been helped by this foundation. The Rockefeller Foundation, mainly because of Banting's work, gave the University of Toronto $1,000,000 as an endowment for the Faculty of Medicine. The service of an unpaid assistant and the use of a small laboratory and ten dogs profited greatly the University of Toronto.

IV

"Love is the master key that opens the gates of happiness, of hatred, of jealousy and, most easily of all, the gate of fear."—Dr. O. W. Holmes

The fourth part of this story concerns the domestic life of Banting which, until 1923, consisted mainly of living in small one room quarters with occasional flings at romance. In his undergraduate years he had little enthusiasm for parties or dances. During the war and shortly after, he had a romance that ended with Banting being possessor of the diamond rather than the girl. However, he now commenced to show some interest in a Miss Marion Robertson who worked first at Christie Street Hospital and then at the radiology department of the Toronto General Hospital. This friendship changed to a romance and they were married on June 4, 1924. Banting was scheduled to speak in July 1924 at a conference on Health Problems in Tropical America sponsored by the United Fruit Company. The Company presented the newlyweds with a cruise from New York to the Carribean and back, looking after them while they were in Jamaica attending the conference. This

was a pleasant interlude and a very happy time for them both. When they returned, an attractive new home was ready for them on Bedford Road.

Banting and his wife travelled to Europe in 1925 where they were received royally. In 1926 they journeyed to the Canadian West. All these trips were for medical meetings, the European jaunt to allow him to deliver his Nobel Address. These were happy years for Banting and his wife, but people could see an incompatibility creeping into their lives. In April of 1929 William Robertson Banting was born and added a new part to Banting's life. He was very fond and attached to his only child.

Banting had a generous personality, but at times he would be stiff and strangely unsympathetic. Anyone seeing him on these days would do better to come back some other day. His disappointments and worries unfortunately showed in his social behaviour. In his early days he had a peptic ulcer, but as he realized his ideas it quieted down. However, towards 1930 it commenced to exacerbate again as did his moods which some described as sweet and smiling, others dour and difficult.

Banting was fond of simple and plainly spoken people who took life in moderation. He did not have great numbers of intimate friends, but those that he did have formed a varied group with one basic characteristic—simplicity. He shunned society in its narrow sense. He hated hostesses who catered to personalities, and if forced to mingle in such a group his manner was very cool. He loved to be in the outdoors. Whether in the simplicity of his likes, his determined nature, his devotion to science there was a factor that was incompatible with his wife it is difficult to say. On April 25, 1932, a divorce was granted to Banting, that as well gave him custody of his child, thus ending a period of intense strain in his life.

His moody behaviour that had been getting more marked in this period was now very marked. He seldom went out, and when he did it was mainly with his friends from the Arts and Letters Club. Gradually the fold of science enveloped him again and he became his more usual personality.

V

"One must act in painting as in life, directly."—Picasso

Banting, who had shown some ability as an artist in his youth, found a release for his skill as an adult. He became a member of the Arts and Letters Club of Toronto which included the famed Group of Seven of whom A. Y. Jackson became his friend and counsellor in art. Banting loved to go to Quebec or Georgian Bay with Jackson to paint for a period of days or weeks. The influence of the master painter on the amateur became very marked, and some authorities in the world of art could not tell Banting's better works from those of A. Y. Jackson.

One of their more dramatic expeditions was into the Arctic on the government supply ship Beothic. Jackson had been appointed by the government to go on this trip, and it was only through the thoughtfulness of a civil servant in Ottawa that Banting was allowed to go as an investigator of Eskimo health. The two men had much pleasure painting the rugged scenery, but Banting also stuck to his task and found that the great fur trading company in this area was indirectly undermining the health

of the natives. His study which was done with his usual thoroughness, was going to cause some changes in the north.

While returning to Toronto Banting was accompanied by a reporter from a Toronto daily paper who took part in a discussion between Banting and Vincent Massey of the northern findings. Although specifically requested to withhold this information until the report was made public by the proper authorities, the reporter did not do so, and the next edition of his newspaper carried a full account written so that the company involved seemed wholly responsible for the condition of the Eskimoes. Banting was disgusted at this paper's lack of morals, but fortunately, the whole matter was settled amicably as far as Banting, the Canadian Government and the company were concerned. Banting's animosity for this journal was further increased when it smeared his divorce proceedings on its front pages.

Another incident relating to this Arctic trip followed an account of his journey in the May, 1930 edition of the Canadian Geographical Journal. Vilhjalmur Stefansson in his iconoclastic book *Adventures in Error* picked out errors of many great men including Banting. From Banting's Geographic article he took many statements, one of which was "In a country where there is no sunshine for three months of the year, the people are dependent on food for their vitamins," to which Stefansson replied, "The inference seems to be that if there were more sunshine these remarkable people would not have to depend on food for any of their vitamins. The recipient of one Nobel Prize for endocrine studies may then well be candidate for another in comparative racial physiology and in deficiency disease." Stefansson's point in his book was that from many eminent and respected men, misinformation is sometimes given out to be readily accepted by an uncritical world.

VI

"We have never hired a person to do experimental work, but we do hire people who want to do experimental work. They and they alone, are the research workers who will eventually pay dividends."—BANTING

The lessons which Banting learned while working on the insulin problem governed his actions when he became Professor of Medical Research in 1923. Banting and his workers occupied three rooms in the Pathology Building which is now the Dunlap Building. All the departments of the Faculty of Medicine were as cramped so the Banting Institute was planned to contain the Departments of Pathology, Pathological Chemistry, Bacteriology, clinical laboratories and the Department of Medical Research. The funds were raised mainly through the generosity of the Provincial Government. The construction commenced on November 21, 1928, and the opening by Lord Moynihan of Leeds, President of the Royal College of Surgeons took place on September 16, 1930.

Banting settled into a life of administering his own department and carrying out what projects of his own there was time left for him to do. His dream of a research worker embodied most of his own characteristics and experiences. He bent over backwards as a democratic and considerate head of his department, taking utmost care to avoid what had

happened when Dr. MacLeod's old German protocol had so annoyed him.

He had an immense power of simplification, and when confronted by problems about which he knew little, they were stripped to their essentials in order that he might understand them. Although he appreciated the necessity of scientific words, he held little respect for the man who cloaked his ideas in a multitude of high sounding words. As with all men who are intelligent he was not afraid to admit his own ignorance, but even when he knew little about a problem his questions sometimes left the experts wondering at their own ignorance.

He picked the men who worked in his department for their imagination, discipline and love of research. He encouraged his associates to further their knowledge by taking worthwhile postgraduate training, not for the sake of degrees, but for their own mental benefit. Banting was very much impressed by the mind of a Mr. Hall from the Ontario Agriculture College and soon had him employed in the Department of Medical Research. He eventually persuaded Hall to take a much accelerated course in Medicine which he easily passed. (The Faculty has since made it impossible for anyone to take Medicine in such a short time.) Hall soon became Banting's immediate assistant and was groomed as administrator to allow Banting more time for research. He later became Dean of Medicine at the University of Western Ontario, and when he became President of that University, he was succeeded by Dr. Collip.

The work performed during Banting's tenure here was varied, including such things as research in cancer, myocardial infarction, properties of blood serum, intestinal intoxication, and others. One of particular interest to Banting was the problem of silicosis. Here the mining industry, the Provincial Department of Industrial Hygiene and the Banting and Best Department of Medical Research collaborated and made considerable progress with this problem.

In 1935 Banting was made a member of the National Research Council and in 1938 was made Chairman of the Associate Committee on Medical Research which he founded. It was with this group that he was to play an important part when war came in 1939.

The International Physiological Conference under Pavlov was held in Moscow in 1935 and Banting who attended found time to see some of the Soviet Union. His enthusiasm for the new order was tremendous, and he returned greatly impressed with what the Russians had accomplished. To him their great use of science and the aid given to scientists was almost unbelievable. Not even the most avid Communist could have written the glowing phrases which he did on his return: "All people have the opportunity to rise as high as their talents and industry will permit in whatever field of endeavour they may select. Every person's future is invested in the state. The state in turn provides for the education of children and an old-age pension. This sense of security brings happiness and peace of mind and permits true culture" (*Science and the Soviet Union*).

In the fall of 1938 when he had assumed Chairmanship of the Medical Research Committee, he went on a tour of the Dominion to investigate the facilities for medical research in large and small centres. This was completed early

in 1939, and his thorough work provided a basis for the allotment of the National Research Council grants.

In June of 1939 Banting was married to Miss Henrietta Bell, a graduate of Mount Allison University who had been working at the Banting Institute. This was the last interlude of peace that Banting had before the onset of the war.

VII

WAR

Nine days before Canada declared war, Banting became a pathologist with a newly organized medical unit. He was persuaded by his superiors that he would be of more value looking after Canada's wartime medical research. This he reluctantly accepted. As well as being Chairman of the Associate Committee on Medical Research, he was attached to National Defence Headquarters in the position of Director General of Medical Services. To obtain first hand knowledge for Canada's wartime medical research programme he went to England in the winter of 1939-40.

The staff at Toronto now supplemented with some prominent research men from the United States of America undertook work in the field of fatigue in air personnel, anti-blackout suits, a portable oxygen apparatus and other problems. The decompression chamber built at the Banting Institute to study high altitude effects found as its first occupant Sir Frederick, who stayed for one hour at 40,000 feet. Although tremendously busy with his heavy administrative work, he still found time to partake of some of the research. Towards the end of 1940 Banting thought that there was need of a further visit to England to observe the changes and advancements in war research. Hence he proposed a flight to Europe in February of 1941.

On February 20, 1941, a Lockheed Hudson patrol bomber being ferried to England took off from Gander airfield in Newfoundland with its crew of three and Sir Frederick. A short while after leaving Gander one engine failed, and the aircraft signalling its home base announced that it was turning back. A bearing was given, then nothing more was heard from it.

When the plane seemed to be over Newfoundland, the pilot ordered everyone to jump and parachute to safety. After he thought that this had been done he proceeded to attempt a landing in the dark and snowy night on the barren wastes of Newfoundland. Since half of Newfoundland is lakes, his chances of setting the plane down in the deep snow were good. However, the only big tree in the area caught one wing and the plane crashed on the snow covered tundra. When the pilot regained consciousness he found the remaining crew members dead and Sir Frederick alive but seriously injured. Banting never regained consciousness and died twenty hours later. On February 25th the wreck was spotted and the pilot rescued. At autopsy in the Banting Institute Dr. W. T. Robinson expressed the opinion that had medical aid reached Banting immediately he would have had a chance to live.

His life is an example of how the desire to achieve can surmount all obstacles. Banting was not a brilliant scientist in the terms of a trained scientist: instead he was a man who guided science and

simplified its cumbersome problems. He was a man of complex character who, to those who knew him well had a dominant trend towards a humble simplicity.

ACKNOWLEDGEMENT

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BAL AND METAL POISONING

M. J. WEISENBERG, 5T3

Historical Review

The development of BAL is so intimately related to the problem of arsenic poisoning that it is virtually impossible to discuss one without the other. Arsenic compounds are sufficiently widely used commercially to be a frequent cause of poisoning, and the toxicity of these compounds has been recognized for hundreds of years. More recently arsenic has been used therapeutically, especially in the treatment of syphilis, and here toxic manifestations are far from infrequent. Arsenic poisoning most commonly presents one or more of the following symptoms; an intense gastro-enteritis, a dermatitis, neurological disturbances, blood dyscrasias and renal failure (arsine).

Various research workers have established that arsenic acts by interference with certain enzyme systems in the tissues of the victim, and in 1907 Heffter, and later Erlich and others showed that the toxic arsenoxides react with the sulphydryl groups in these enzyme systems. It was also established that this could be counteracted by the administration of certain compounds containing these groups, such as glutathione and thioglycollic acid, and that these monothiols, that is, compounds with a single sulphydryl group, exert a protective action by competing with the sulphydryl groups of the tissue components for the arsenic. Later work showed that one arsenic molecule combines with two sulphydryl groups, and that dithiols were more effective than monothiols.

When the possibility of the use of arsenical war gases such as lewisite arose, a group working at Oxford under Peters sought an antidote and found the dithiol, 2,3-dimercaptopropanol to be the most effective. The name BAL or British Anti-Lewisite was proposed by American workers who had mistakenly carried out confirmatory experiments using the much more toxic 1,3-dimercaptopropanol. Their comment was that Lewisite was in fact an excellent antidote for the so-called British Anti-Lewisite. BAL was soon tried clinically, chiefly in cases of arsenical dermatitis occurring during therapy for syphilis. Recovery occurred in one-quarter to one-half of the usual time, in 80–85% of cases. Early adequate treatment was also found effective in about 85% of cases of arsenical encephalitis.

Preparations

BAL is commercially available under the official name, Dimercaprol Injection U.S.P. as a 10% preparation in benzyl benzoate and peanut oil, suitable for intramuscular injection. BAL in itself is sparingly soluble in water, 1:15, and may be used orally. In cases of dermatitis it may be applied topically in jelly form, with due regard for the possibility of absorption of toxic quantities from raw areas.

Pharmacology

Many enzymes containing the sulphydryl group are inhibited by heavy metals and it is by the reversal of this inhibition

that BAL exerts its therapeutic effect. Moreover, BAL itself is a powerful inhibitor of a number of metal containing enzymes and acts by combining with the metal of the prosthetic group. BAL and other mercaptans are also powerful reducing agents and can destroy the physiological action of insulin, prolong the prothrombin time, destroy such iron porphyrin compounds as haemin and oxyhaemoglobin by opening the porphyrin ring, and inhibit tissue oxidation as a whole.

BAL is not preferentially stored in any organ but is rapidly excreted in the urine in slightly modified form or in combination with the heavy metals

The usual dose of BAL is 0.2 Gm. intramuscularly. The toxic dose varies from 3–5 mg. per kilogram of body weight, and the effects of these doses last only an hour or two and are fully reversible. While a single dose of 8 mg./kg. gives rise to marked toxic symptoms, doses of 5 mg./kg. may be repeated every three hours during one day without significant cumulation.

The manifestations of the toxicity of BAL are many and varied. Topical application of therapeutic doses produces no systemic manifestations and only transient local wheals. With intramuscular administration, toxic effects are very common and include most frequently nausea, vomiting, headache, burning sensations in the mouth and throat, salivation, abdominal pain, tearing, elevation of blood pressure, and general agitation in addition to pain at the site of injection. These manifestations generally disappear within two hours of the injection. There is no systemic sensitization although the skin may become sensitized to topical applications and react with the production of an area of edema and erythema, and occasionally some papules, these lasting upwards of forty-eight hours. Gross overdoses of BAL result in convulsions and death; the convulsions may be controlled with sodium pentobarbital.

Clinical Applications and Experimental Observations

ARSENIC

BAL has proven to be exceedingly useful in the treatment of arsenical dermatitis and encephalitis, and also some of the post-arsenical blood dyscrasias including thrombopenia and thrombocytopenic purpura. Many cases of arsenic poisoning seem also to be suffering from a Vitamin B_1 deficiency, and some investigators feel that in the case of a reaction to arsenic therapy Vitamin B_1 should be used as well as BAL. BAL suppresses the action of arsenical drugs and increases the time required to clear the blood of spirochaetes.

MERCURY

BAL is exceedingly effective in mercury poisoning, but only if it is used immediately. A series has been reported in which administration of BAL within four hours of the ingestion of the mercuric chloride resulted in twenty-four recoveries without a single fatality. It is interesting to note that the administration of BAL inhibits the action of the mercurial diuretics.

CADMIUM

Experiments performed here by MacFarland in 1949 showed that BAL is very effective in reducing the mortality due to cadmium poisoning, but that maximum protection was obtained over a narrow dosage range, and that even

a very slight excess of BAL leads to a marked decrease in survival rates.

GOLD

BAL is effective in the treatment of the dermatides, purpura, and granulopenia which occasionally occur in gold therapy for arthritis, but the arthritic symptoms are likely to recur.

Animal experiments would seem to indicate that BAL is useful, also, in the treatment of poisoning with antimony, bismuth, copper, nickel and tungsten. The use of BAL is contradicted in poisoning with uranium, silver, cobalt, selenium, iron, lead and chromium. Its affinity for lead is not sufficient to prevent the ionization of the lead which it removes from the bones and the symptoms are often aggravated. In the case of chromium intoxication, MacFarland found that the use of BAL caused a marked decrease in the survival time.

CONCLUSION

BAL is an extremely useful drug in the therapy of intoxication by arsenic, mercury, gold, antimony, bismuth, copper, nickel, and tungsten, and early adequate therapy with this drug reduces mortality figures to a very satisfactory level indeed. Its use is contraindicated in poisoning with lead, chromium, uranium, silver, cobalt, selenium and iron. In these cases it has no beneficial effect and may increase the toxicity of the metals.

ACKNOWLEDGEMENT

The author wishes to thank Prof. J. K. W. Ferguson of the Dept. of Pharmacology for his encouragement and assistance in the preparation of this article.

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2. Modell, Gold, and Catell: Journal of Clinical Investigation No. 4, Vol. XXV.
3. MacFarland, H. N.: The Use of BAL in Heavy Metal Poisoning. Ph.D. Thesis. U of T, 1949.

MEDICAL ALUMNI ASSOCIATION BURSARIES

Students of the Medical Years are encouraged to consider application for these bursaries of which there are four of the value of $100 each. Preference is given to male students and the following considerations are the basis of the award:

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CASE REPORTS

J. K. C. MURRAY, 5T3

Case No. 1: L. B., an eighty-four year old male.

Chief Complaint: Intermittent severe gastric and umbilical pain of two weeks' duration.

History of Present Illness: Two weeks before admission, patient began to have intermittent pain in the epigastrium and around the umbilicus of gradually increasing severity. The pain came on after meals and later became independent of meals, coming on about 3.00–4.00 a.m. He had anorexia, nausea and grey emesis at intervals frequently after meals. He had lost ten pounds in weight during the past few weeks, and two days before admission he had noticed tarry stools for the first time.

Personal History: Patient had been a railway employee, but later was in the hotel business with his brother. He was unmarried and lived with his sister, but since her death has been living alone. He does not smoke or drink.

Family History: Mother died at seventy-eight of heart attack; father was killed in an accident. No history of carcinoma, diabetes or heart disease.

Past History: Four years ago patient was admitted to hospital with a complaint of pain in right upper quadrant of one week's duration. Three weeks before this he had noticed frequency of urination with slow stream and foul smelling urine. One week previous to admission he developed severe right upper quadrant pain. He did not vomit although he felt distended. The bowels moved the next day with a laxative, but the feeling of fullness in the abdomen continued.

Physical examination revealed a distended abdomen and a palpable mass thought to be gall bladder. Diagnosis was subacute cholecystitis with stones. Operation was thought inadvisable because of age (eighty years), and patient remained in hospital four months.

During his stay in hospital he had occasional attacks of nausea, vomiting and right upper quadrant pain. He also had phlebitis in both legs after the first month. During the first week the temperature showed spikes as high as 100°F., but after this it rarely was above normal.

He was dismissed and advised not to eat fatty or greasy foods, and was better for a few weeks. However, his pain became worse and was not relieved by food.

Two years before his final admission, he was admitted complaining of a sharp, piercing pain in the epigastrium and gall bladder region radiating across the front of the abdomen to both sides, and accompanied by nausea and vomiting.

He was admitted twenty months later for a similar complaint.

Physical Examination: Essentially negative except for right upper quadrant tenderness on deep palpation and some rigidity below the costal margin.

Discussion: Under sedative, pain was gradually alleviated, but four days later he vomited "coffee ground" material. He was given transfusion, but vomitus was now bright red, and tarry stools were frequent. Patient died five days after admission.

Pathological Findings:

(1) Large chronic duodenal ulcer based on pancreas with eroded arteries at the base, and profuse haemorrhage into the intestine.

(2) Acute oligemia.

(3) No cholecystitis or cholelithiasis.

(4) Distended but unruptured abdominal and oesophageal veins.

(5) Moderate aortic atherosclerosis, marked coronary sclerosis with myocardial scarring.

* * *

Case No. 2: A. R., a twenty-one year old male.

Chief Complaint: Lower abdominal pain of six months' duration.

History of Present Illness: This twenty-one year old white medical student who had been in good health was troubled towards the end of October, 1944, by "nagging" abdominal pain in the right lower quadrant. There was no nausea, vomiting or bowel disturbance, but there was slight tenderness to deep palpation over the appendix area. After three or four days the pain subsided, and the patient felt perfectly well.

One week later while in a movie, he found himself unable to keep warm in spite of gloves and an overcoat. On reaching home he had a severe headache so that he took ten grains of aspirin and went to bed. In the morning the headache had disappeared, but severe nausea and localized abdominal pain prevented him from eating breakfast. He again was unable to keep warm, and went to the hospital where he was admitted, his temperature was 101°F. In two hours his temperature was 104°F., and severe headache and photophobia were present. Leucocyte count was 12,500, 88% polymorphs. In view of the high temperature and slight abdominal signs, appendicitis was ruled out: lumbar puncture was done which was negative. Blood and urine cultures and chest X-rays also were negative. Patient was treated with sulphadiazine, and his temperature fell to normal within a week. He was sent home at the end of November, undiagnosed.

For the next six months the right sided abdominal pain recurred, gradually becoming less severe and less frequent.

In April, 1945, a firm, enlarged gland appeared in front of the left ear, followed a week later by one in front of the right ear. There was no constitutional disturbance to suggest mumps, and a chest X-ray and Mantoux test 1:10,000 were negative.

In May he became aware of a glare in the left eye which two days later was observed to be inflamed and reddened. Vision was somewhat clouded, but there was no pain. Diagnosis was superficial keratitis punctata, and patient was treated with eye drops and later X-ray. This had no effect, and short wave therapy was advised—diagnosis was now irido-cyclitis with synechiae, and atropine drops were ordered.

Various consultants such as dental surgeons, radiologists, oto-laryngologists and abdominal surgeons were now called in, but no diagnosis could be made.

Barium enema revealed a short appendix adherent to the caecum which was mobile. There was some ileo-caecal tenderness.

In July the E.S.R. was 45 mm. per hour, and patient was readmitted to hospital. The X-ray of the chest at the time showed increased hilar shadows and suggested glandular enlargement.

At this time there were no symptoms referable to the chest—no cough, sputum or shortness of breath. The heart and lungs were normal and there was no undue sweating, the temperature and pulse being normal. Tenderness to deep

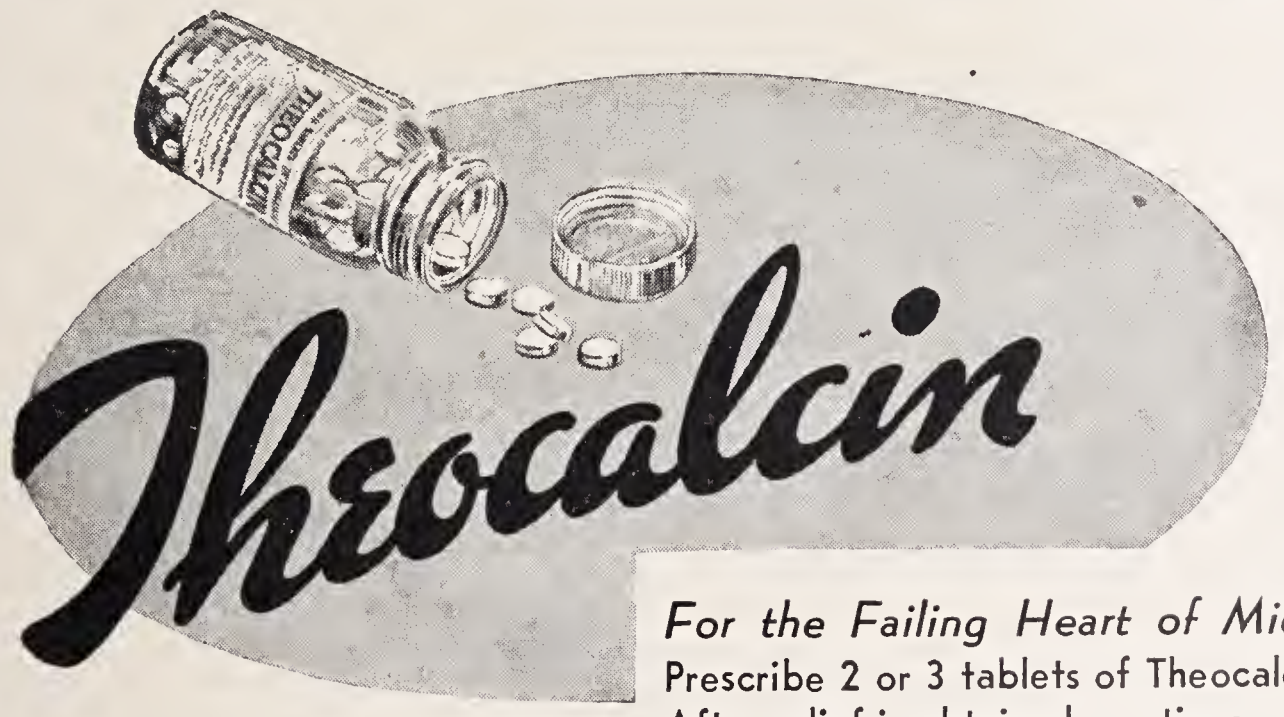
pressure was still present in the right lower quadrant, but neither spleen nor liver were enlarged. The right eye was normal, but the left eye was red owing to circumcorneal injection, and the pupil was irregular, dilated by atropine. No evidence of tuberculosis could be found, and six stomach washings revealed no tubercle bacilli. The Mantoux test was negative in dilutions of 1:1,000 and 1:100. The blood findings were: haemoglobin 90%; W.B.C. count 5,500 with polymorphs 61%, lymphocytes 33%, monocytes 1%, eosinophils 3%. Sedimentation rate was 30 mm. per hour.

Discussion: Had this patient been afflicted with recurrent attacks of subacute appendicitis followed by pyrexia of unknown origin, non specific parotitis, irido-cyclitis and mediastinal glandular enlargement or were these all stages in a single disease?

Although the fingernails were not blue-red, and the characteristic punched out or generalized atrophic X-ray picture of sarcoidosis was not present, it was considered to be the diagnosis. The albumin was 3.6 Gm/100 c.c. (normal 3.8 to 5.2 Gm./100 c.c.), and the globulin was 3.8 Gm/100 c.c. (normal 1.6 to 2.8 Gm/100 c.c.).

In sarcoidosis the root glands are usually affected and may be indistinguishable from tuberculous glands on roentgenologic examination. Areas of atelectasis due to pressure on a bronchus may be present.

Since there is no specific treatment for sarcoidosis, the patient left hospital for a period of convalescence. By October the A/G ratio was normal and the left eye had improved considerably, although the chest X-ray findings were unchanged. By December, even the root gland shadows were smaller, and the abdominal pain had not recurred.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ABSTRACTS

SURGERY

A Histological Explanation for the Beneficial Action of Endocrine Therapy in Carcinoma of the Prostrate: Nicol, T., Helmy, I. D. and Abowzikry, A. British Journal of Surgery, Vol. 40, 166–172, 1952.

The authors, knowing that fibrosis follows the endocrine and the castration treatment of cancer, that the reticuloendothelial system has an important part in the body's protection against cancer, and that a genetic relationship exists between reticuloendothelial cells and fibroblasts, decided to study the effect of oestrogens on the reticuloendothelial system and the part this system may have in prostatic fibrosis.

Various oestrogen preparations were administered to intact male, to orchidectomized, and to ovarectomized guinea pigs, and vital stains given to stain the reticuloendothelial cells. It was found that both orchidectomy and oestrogen therapy stimulated the reticuloendothelial macrophages in the spleen, liver, and lymph nodes, but that oestrogen therapy caused a greater degree of mobilization of these cells in the circulation and of their accumulation in the secondary sex organs, especially in the prostate. The effect was greater when the two methods were combined. The macrophages in the prostate may be formed in situ, but it is more likely that they are derived from the reticuloendothelial system. With prolonged oestrogen therapy there was fibrosis in the prostate, probably due to the transformation of the macrophages into fibroblasts.

As a result of this experiment the authors recommend that an investigation be undertaken to find a substance with the same action as that described herein for oestrogen, but with fewer of its ill effects.

L. Grainer

PEDIATRICS

The Treatment of Acute Leukemia in Children With and Without Folic Acid Antagonists: Poucker, H. G., et al., Journal of Pediatrics, Vol. 41, No. 4, 1952.

Thirty-eight cases of acute leukemia treated with folic acid antagonists are compared with forty-eight cases treated with various agents before the advent of the antagonists. The mean duration of life was significantly increased from 22.9 weeks in the pre-antagonist group to 48 weeks in the antagonist-treated group. Temporary bone-marrow remission, lasting an average of 9.4 months during which apparently normal red and white blood cells were produced, occurred in 12 of the antagonist-treated cases. Even in cases without bone marrow reversion there was often striking clinical improvement. This was judged by increased appetite, decreased fever, decreased abdominal and bone pain, and decreased size of spleen, liver, and lymph nodes. In pre-antagonist days bone marrow improvement was reported in the literature only rarely.

Antagonist treatment was started with Aminopterin, and if necessary, was continued with the less toxic but less effective A-methopterin. Early treatment appeared to favour a better response, but there were always relapses with successively decreasing response to therapy. Antibiotics did not alter the course of the disease.

The folic acid antagonists do not cause aplasia of the bone marrow, but act on the co-enzymes which ensure the maturation of white blood cells. Folic acid and the more active citrovorum are fractions of these co-enzymes, but their method of action is not clear. Excess folic acid alone apparently does not cause leukemia. The folic acid antagonists offer an approach to the further study of the cause of leukemia.

M. S. Kazdan

NEWS AND NOTES

Medical Society

The Medical At Home for 1953 is to be held at the Royal York Hotel, on the night of February 18th, at 9 o'clock. "Internel Medicine" is to be the theme of the dance and the "plight" of the lowly interne is to be satirized in both entertainment and decorations.

Benny Lewis' orchestra has been engaged for the Concert Hall and Cy McLean's group will play in the Crystal Ballroom.

Organization of the entertainment for the evening is under the able direction of Doug. Salmon, Meds 5T5, who has a committee working with him composed of representatives from most of the years. Although it will have a medical theme, the floor show should be appreciated by the entire audience.

This year, chairs will be provided for those near the stage and, in this way, visibility should be greatly improved.

The decorations are being directed by Don Cowan, Meds 5T6, who has a committee of interested and talented people working with him. The colourful murals which have made the Meds-at-Home famous will grace the walls of the Concert Hall once again, and will reflect the general theme. The Crystal Ballroom will be transformed into New Orleans for the evening, replete with an old wharf, streetlamps, and tables arranged in cabaret style.

If these plans are any criterion, we can certainly look forward to a most enjoyable evening.

* * *

The new crest of the Faculty of Medicine will go on sale to all medical students in the first two weeks of January. It will be sold by Henry Birks Company suitable for blazer wear and on pins and rings. The price will be ten dollars for the blazer crest or nine dollars to groups of six or more. The design may be seen on the front cover of the Journal.

The campaign to raise funds for SHARE (the organization which is giving aid in the form of books and financial support to Asian university students), is being continued again this year. Personal canvassing of students was carried on during the week of November 28–December 5. The chairman in charge of canvassing this year is Harvey Tonken of Meds 5T5. All the representatives of SHARE in the premedical and medical years are to be congratulated on their fine piece of work.

* * *

Medical Athletics

This year the Meds football team regained some of the spirit and ability that characterized the Meds teams of former years. Under the able coaching of Ross McKelvey of Queen's University football fame, they were the only team to give this year's Mulock Cup Champions, Victoria College, a good battle. Unfortunately, Victoria won the game 8–7.

Members of the team included Gaviller, Jackson, Cecutti, Bowles, Pace, Mustard, Murray, Harris, Van Nostrand, Bull, Noonan, Rundle, Irwin, Stuparyk, Hotti, Lawden, King, Baida, Barrington, Forstner, Wheeler, Steeman, Bate, Stalker, Webber, Stipee, Balland, Kerr, Hutchison, Pickering, Martin, and Copolino.

* * *

Women's Athletics have been active this year. The girls entered a baseball team and two basketball teams, which all did very well in their respective leagues.

Their hockey team is now busy practising in an effort to retain the intramural cup which they won last year and promise to have a strong contender in the intramural league.

* * *

M.W.U.A.

The Medical Women's Undergraduate Association held a forum at the School of Nursing on November 18. The speakers

were Dr. M. M. Brown, Dr. Frank Griffin and Dr. G. Hatcher who spoke on Public Health, Industrial Medicine, and general practice in Saskatchewan respectively. All those attending agreed on the success of the forum.

* * *

The staff of the Women's College Hospital held a tea on December 5 for all the women undergraduates in honour of the girls in the first pre-medical year.

* * *

C.A.M.S.I.

Films of interest to medical students are again being shown every Wednesday from 1–2 o'clock in the lecture-room at the Banting Institute. These films which are presented under the auspices of CAMSI cover a wide variety of subjects and students are reminded to take advantage of this service.

* * *

Faculty

Drs. J. K. W. Ferguson, G. H. W. Lucas, E. J. Martin, W. Paul, W. Kalow, A. Dyer, J. Parker and J. McCall of the Department of Pharmacology attended meetings of the Canadian Physiological Society in Quebec, which were held on October 10th and 11th.

Dr. P. E. Ireland, Professor and Head of the Department of Oto-laryngology, was in Chicago from October 6 to 17 attending the meetings of the American Board of Otolaryngology and the American Academy of Laryngology.

Mr. Harold Ridley of St. Thomas' Hospital, London, was a visitor to the Department of Ophthalmology on November 3. He spoke at the Academy of Medicine on "Intra-ocular Acrylic Lenses."

* * *

Medical Alumni Association

The seventh annual Graduate Meeting of the Medical Alumni Association of the University of Toronto was held at the new Osler Hall (Academy of Medicine) on October 16 and 17.

The Staff was very well represented on the programme which included twenty-four papers and four round table discussions. The subjects of the round table discussions were: Thyroid Disease, Painful Shoulder, Biliary Disease, and Diabetes in Pregnancy.

* * *

The September issue of the Archivos Médicos de Cuba, a well-known medical journal in that area of the western hemisphere, was dedicated to the University of Toronto. Among the members of the Staff contributing articles to the issue were Drs. Hardolph Wasteneys, E. B. Tovee, W. F. Greenwood, A. D. McKelvey, A. B. Stokes, C. H. Best, C. C. Lucas, J. H. Ridout, J. A. Dauphinee, W. T. W. Clarke, D. E. Cannell, W. J. McGarrity. On the frontispiece to the issue was our new faculty crest.

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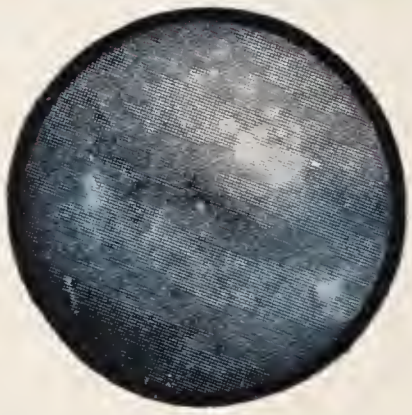

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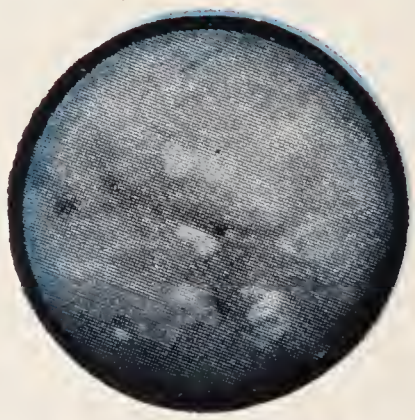

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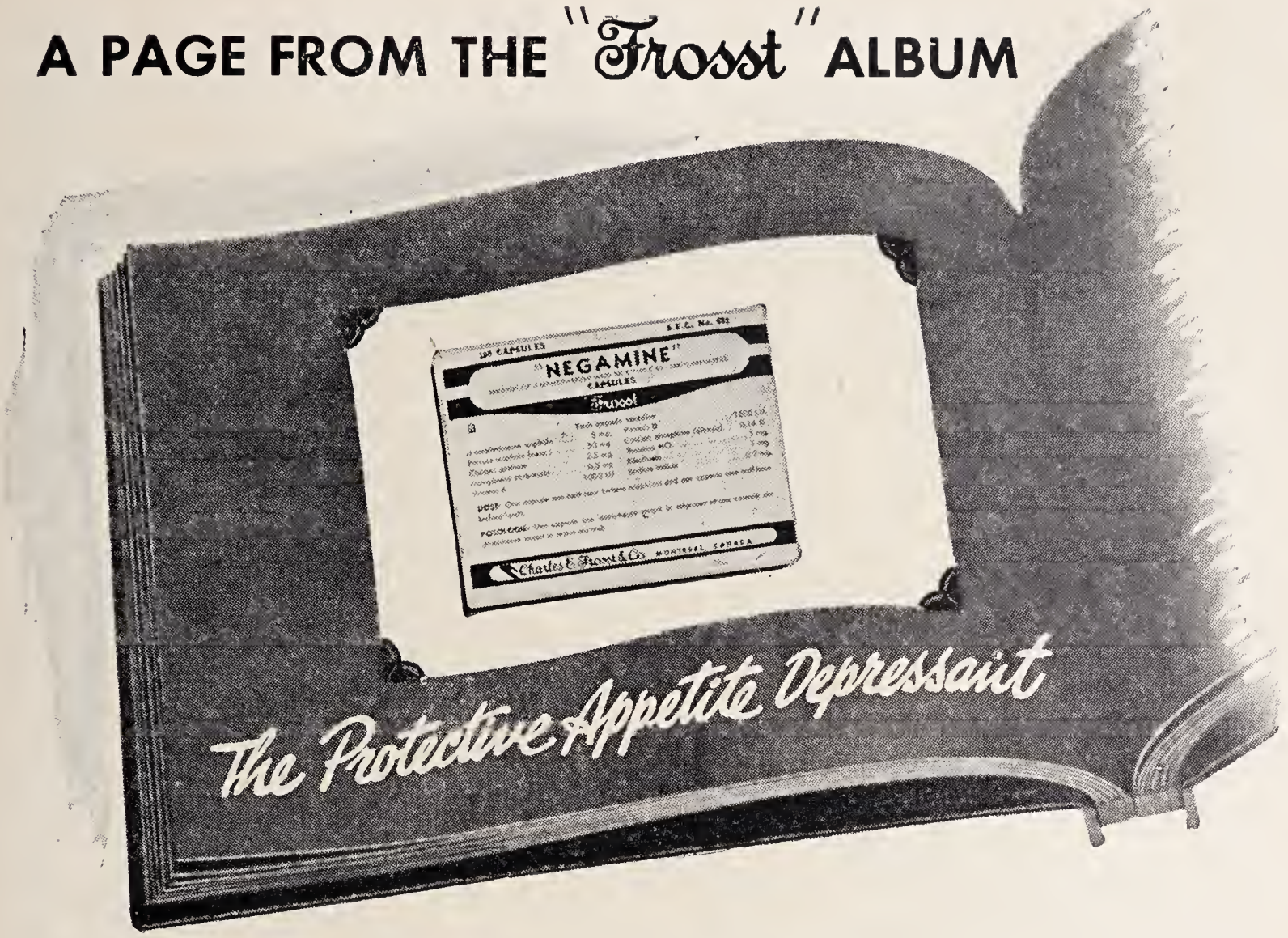

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Otitis media (streptococcal)	B	A		B	B	

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Crystalline Vitamin B_{12}	20 micrograms
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